

# Van den Ende Memorial Lecture

## CONTRIBUTIONS BY YOUNG MEN TO MEDICINE

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It is a great compliment to have been asked to deliver the van den Ende Memorial Lecture instituted in this medical school. The name which we commemorate today conjures up in our minds a friend and colleague who had many fine attributes. Among these is the fact that he was a scientist with a deep love for his subject, who, early in his medical career, showed ability as a research worker.

In choosing a subject for this memorial lecture there came to mind certain individuals who are famous for the outstanding and far-reaching contributions they made to medical science and who made discoveries very early in life. This topic is the main theme of my address.

Outside the medical profession there are well-known examples of brilliant young men whose names will live forever. For instance, in the realm of music there are a number of composers who were outstanding in their youth. Mozart at the age of 5 years wrote an incomparable piano concerto. This great musician lived only to the age of 35 years. Franz Liszt, when 10 years old, already played with the technique and the emotion of a mature virtuoso. Brahms, who was born in the slum districts of Hamburg, was something of a child prodigy. Chopin, who was very ill with tuberculosis at 20, had composed a great deal before this age; he died when he was 40. Schubert died at 31 and Mendelssohn at 38.

Examples from the physical sciences include the following: Copernicus (1473-1543), the famous astronomer, was appointed to the chair of astronomy in the University of Rome at the age of 26. Galileo (1564-1642), who was intended to devote his time to medicine, studied Euclid and turned his mind to geometry and philosophy. He made important discoveries before he became professor of mathematics at the age of 24 years at the University of Pisa. Isaac Newton (1642-1727), at 24, had discovered the binomial theorem and the principles of the integral calculus. He was appointed to full professorship in mathematics at Cambridge University when he was 27. Thomas Edison (1847-1931), the great inventor, received 40,000 dollars at the age of 23 years for one of his first inventions—the Edison Universal telegraphic printer. Guglielmo Marconi (1874-1937), at the age of 22 years, patented his new system of signalling—the world's first patent for wireless telegraphy. Svante Arrhenius (1859-1927), at the age of 24, read his preliminary paper which, with van 't Hoff's note, forms the basis of the modern conception of electrolyte dissociation and of osmotic pressure. Albert Einstein (1879-1955) published his Theory of Relativity when he was 26 years old.

In the history of medicine there are records of discoveries made by old and young. There are, however, few recorded instances of epoch-making discoveries by very young men, of the age of the medical student at present-day universities.

### CONTRIBUTIONS TO MEDICINE

Examples will now be given of men well known in the history of medicine who made important discoveries early in life.<sup>1,2,4,6,7</sup> For the sake of interest and to limit the number considered, the age limit has been set at 26 years. With this limitation the discoveries of only twenty-three scientists, most of them well known to the medical profession, will be presented briefly. Some of the individuals to be mentioned have gained recognition through their assistance in team work, but most appear to have made important original contributions on their own.

Niels Stensen (1638-1686) made important contributions to anatomy at an early age. He discovered, when he was 22 years old (while dissecting the head of a sheep in the house of his professor),

that he could pass a probe down a channel from the parotid gland. This was the parotid duct (Stensen's duct). He afterwards examined other glands such as the lacrimal glands, and was able to prove that all externally secreting glands have ducts. His contributions are so amazing as to be almost unbelievable. He described Peyer's patches and Fallopi's tetralogy before these were re-described by the men whose names they now bear.

Regner de Graaf (1641-1673) was a pioneer in the study of pancreatic secretion. He experimented at the age of 23 on the living dog, and used a goose-quill to construct an external pancreatic fistula. He also dissected rabbits at varying intervals after coitus, discovered the corpus luteum, and traced the passage of the ova down the oviducts to the uterus. His epoch-making discoveries on ovulation were based on experiments performed on more than 100 rabbits and 40 goats, cows, dogs, cats, and other animals. At an earlier date he published a treatise on the male reproductive system. Among his fellow students at Leyden University was Niels Stensen. de Graaf never held an academic post, apparently because he was a Catholic.

Lorenzo Bellini (1643-1704), the Italian anatomist, was born of a poor family in Florence, but showed such promise that Duke Ferdinand II paid for his education. At the age of 20 he became professor of philosophy and of theoretical medicine at Pisa, and later in the same year, of anatomy as well. He is especially known for his classical description, at the age of 18 years, of the gross anatomy of the kidney, which he showed was a conglomerate of tubules including the renal excretory ducts, since known as the ducts of Bellini.

180 years later William Bowman (1816-1892), at the age of 26 years, published his report on the structure and function of the Malpighian bodies of the kidney, including Bowman's capsule which is named after him. He would have been greatly interested in the latest detailed descriptions of the structure of the capsule.

John Mayow (1643-1679), one of several famous Oxford physiologists, is best known for defining, at the age of 23, as a definite chemical entity (spiritus nitro-aereus), the substance we now know as oxygen. He concluded that the purpose of breathing is to take a fraction of air into blood as life-giving 'particles'.<sup>8</sup> He was a shy young man, easily hurt, and the failure of his contemporaries to appreciate his work might have been a factor in causing his early and unhappy death. The full significance of his studies was not recognized until after Lavoisier had announced the discovery of oxygen.<sup>4</sup>

Casper Bartholin the younger (1655-1738) was a member of one of the most celebrated medical families in history; at one stage in their history five of seven sons were professors in the University of Copenhagen. This particular Bartholin is said to have edited and published his father's *Dissertation on the Anatomy of the Swan* when he was 13 years of age. He became a medical student at 16, and three years later, while still a medical student, he was appointed professor of philosophy. At the age of 21 he published a book on the anatomy of the diaphragm. His name is best known to us for his description of the vulvovaginal glands, which are important from the clinical point of view because of their liability to become infected and to form abscesses.

Giovanni Battista Morgagni (1682-1771) was a precocious youth who wrote poetry and discussed problems of philosophy at the early age of 14. He received his medical degree at the age of 19 and devoted himself to anatomy, publishing his first work at the

age of 24. He later became professor of anatomy, but it is for his work *De sedibus et causis morborum per anatomen indagatis libri quinque* (The seats and causes of diseases investigated by anatomy), published in 1761 when he was 79 years of age, that his name is inscribed among the greatest in the history of medicine. He has been called the 'father of pathology'.

Charles Blagden (1748-1820) carried out spectacular and well-conceived experiments in a heated room on the ability of the body to withstand dry heat and the importance of perspiration for maintaining constancy of body temperature. He published an account of his work at the age of 26.

Herbert Mayo (1796-1852), physiologist at Middlesex Hospital, London, clarified the problem of reflex-action, and described the functions of the nerves of the face (motor power in the VIIth, common sensibility in the Vth) in his publication which appeared in 1822. He deserves the credit for this finding instead of Bell, whose name is better known in this connection.<sup>4</sup>

Johannes Peter Muller (1801-1858) was the son of a cobbler, poor but not penniless, who was given a good education and became the greatest physiologist that Germany has produced. He made no epochal discoveries, but he enriched every field he touched. His important contributions to physiology included the important *Handbuch der Physiologie des Menschen*.

He was professor of anatomy and physiology in Berlin for 25 years from the age of 22. He was a great teacher and, unlike Claude Bernard who left no great pupils or disciples, he had pupils who became distinguished, for example Virchow, Helmholtz, Henle, and Schwann.

The ducts (Mullerian ducts) which give rise to female reproductive organs were first noted by him when he was 24.

Hermann L. F. von Helmholtz (1821-1894), a pupil of Muller and one of the greatest thinkers of all time, at 24 years of age measured for the first time the heat production of frog muscle. He had phenomenal powers of sustained abstract thinking. At the age of 26 he had already soared to extraordinary heights, as revealed in the publication of his celebrated essay on the Conservation of Energy. He became professor of physiology at 28. His major achievement was probably in physiological optics, including the mechanism of accommodation and the theory of colour vision. He was a skilled musician, and made contributions to the physiology of hearing.<sup>4,5</sup>

James Syme (1799-1870), the famous surgeon, never attended a course of lectures on surgery while a student at Edinburgh University, and in 1820 while still a final year medical student, 21 years old, he was appointed superintendent of the local fever hospital. He is best known for his amputation operation, essentially a disarticulation at the ankle joint, which he reported in 1844.

Henry Gray (1827-1861), well known to all who have studied anatomy, was lecturer in this subject at St. George's Hospital, London, and had gained prizes and published a number of original papers before he was elected to the Royal Society at the remarkably early age of 25 years. As a student he was a most painstaking and methodical worker, learning anatomy by making dissections for himself. His crowning achievement is of course the well known book, *Anatomy, Descriptive and Applied*, published when he was 31 years old. He died of smallpox at the age of 34.

William Osler (1849-1919), the great medical teacher, who interpreted disease in a functional manner, published many original works. He reported the relation of blood platelets to thrombi when he was 25 years old.

Paul Ehrlich (1854-1915), while still a student, became interested in lead poisoning and devised a stain to demonstrate lead in the tissues. This experiment convinced him that certain tissues had a selective affinity for certain chemicals, an idea which dominated all of his subsequent medical thinking. He described the mast cell at the age of 21 and distinguished it from plasma cells. He published an account of special staining methods for the differentiation of white blood cells and developed the differential blood-count technique when he was 25. His 'side-chain' theory was put forward when he was 31.

Ehrlich's work arose as a by-product of the dye-stuff industry; it laid the foundation of modern haematology and the beginning of a new chemical pharmacology in the provision of remedies which were to foreshadow the triumphs of chemotherapy of this century.

E. Aronsohn and J. Sachs were two medical students at the University of Berlin who demonstrated a centre of control of temperature in the brain in 1884, when they damaged in animals an area adjacent to the corpus striatum. This they showed a few months after Richet in Paris had also produced excessive body temperature by puncturing the brain and producing damage probably in the same region.<sup>2</sup>

Augusta Dejerine-Klumpke (1859-1927) was one of four brilliant sisters of a famous San Francisco family. In their day it was difficult for women to enter the medical profession, but she was accepted in the Medical Faculty of the University of Paris. She was brilliant and, while a student, she described the atrophic paralysis and sensory changes which follow lesions of the lower trunk or medial cord of the brachial plexus (Klumpke's paralysis, 1885). During her final year as a medical student she married the subsequently famous neurologist, Joseph Dejerine.

Walter Bradford Cannon (1871-1945), well known for his analysis of the mechanisms of the internal regulation of body activity (homeostasis), was also a pioneer in radiology. While still a medical student he realized, soon after roentgen rays had been discovered, that they could be used for the study of gastro-intestinal movements. He used bismuth as the radiopaque medium, and the first account of this work was given to the American Physiological Society in 1897.

Jay McLean was a second-year (sophomore) medical student in 1916 working with Howell, the distinguished American physiologist, at Johns Hopkins University. He was assigned the task of isolating certain phosphatides from heart and liver, for study of their thromboplastic effect compared with that of cephalin. Contrary to expectation he discovered an anticoagulant activity in the extracts. The active substance was later named heparin by Howell because of its predominant localization in the liver.

Charles Herbert Best (b. 1899) was associated with F. G. Banting (and J. J. R. Macleod) in the discovery of insulin. Banting was a young Canadian orthopaedic surgeon who obtained a post as demonstrator in physiology and became interested in diabetes mellitus. Best began his partnership with Banting on 16 May 1921, when he was a second-year medical student in the Department of Physiology in Toronto. There was no one in the laboratories at the time they began their work, except the caretaker and one or two friends. It was arranged they should have ten dogs and the use of the laboratory for eight weeks. Mr. Best and Mr. Noble were appointed as assistants to Banting, each to give four weeks. They tossed a coin to decide who would assist in the first four weeks and Mr. Best won the toss. At the end of the four weeks Noble did not return, Best stayed on and was associated throughout the entire work.

On 11 January 1922, eight months after they had begun their experiments, when Banting was 30 and Best 23, the first patients were treated in the Toronto General Hospital with extracts of the pancreas containing insulin, which revolutionized the treatment of diabetes mellitus. This discovery, important in its own way, was also important in giving a fresh and powerful impetus to the study of endocrinology.

Joshua Lederberg (b. 1925) had already made significant contributions to genetics at the age of 21, and with his teacher, Edward Tatum, demonstrated that bacteria have a sort of sex life. At 27 he discovered, in collaboration with one of his own students, that bacteria infected with certain viruses may undergo hereditary changes (transduction) for which discovery he received the Nobel Prize in 1958. He is now interested in exobiology, a new science which attempts to obtain living material from other planets for comparison with that on earth.<sup>6</sup>

The last of the famous young investigators to be mentioned here is Norman Urquhart Meldrum (1907-1933) who died at the age of 26. He isolated the important enzyme carbonic anhydrase which facilitates the reaction between carbon dioxide and water to form carbonic acid. He described its preparation and properties. It is difficult to find any details about him, but his work is regarded as very important since his name and work are mentioned in the book entitled, *Some Founders of Physiology*,<sup>6</sup> which contains a galaxy of famous contributors to the growth of physiology.

The specific medical discoveries which have been cited were epoch-making in that they were milestones which marked new directions for investigators, but the road along these milestones cannot be ignored in realistic medical history.

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Developments in medicine cannot be regarded as taking place in isolation. It must be remembered that they are inextricably bound up with the social process and with scientific developments in other fields. This important aspect is only mentioned in passing and cannot be considered in detail here.<sup>2,8</sup>

The brief account given here of the important discoveries by famous young scientific workers is fascinating and should inspire young people to solve the multitudinous problems which still confront us. The examples that have been cited from medical history should encourage our students to be interested in research at an early age. But research work is not easy and some general remarks on problems concerning the individual and the opportunities in his environment need to be presented.

#### DISCUSSION

##### Chance

Some great discoveries have been made by chance, for example penicillin and mercurial diuretics, but the dictum of Pasteur must be remembered: 'Chance favours the prepared mind'. The discovery of penicillin is often quoted to prove that important discoveries come by chance. The answer is that the particular combination that does the trick does come by chance, but that chance is multiplied by providing opportunities for discovery in the first place, and opportunities for development by interested people in the second.<sup>3</sup> Seemingly trivial accidents have been turned to remarkably good advantage through the ability of an interested and properly equipped person to note nature's slightest deviation from what is expected of her.<sup>5</sup>

##### Hard Work

As a general rule all discovery, even that which at first sight seems to be the result of accident or good luck, is the result of laborious effort, constant and intelligent observation and experiment and, above all, of the individual's ability. Triumph comes to few, and even then it is based on hard work, patience, humility, and the courage to face disappointment and frustration. This is exemplified in the case of drugs which have been produced so abundantly in recent years. While chance still plays a large part in the discovery of new drugs, they are in general produced more rationally. Each new chemical compound is put through a series of tests designed to cover a wide range of pharmacological actions. Technicians, each trained to perform a single test, help to discover whether compounds have any future as drugs. When an interesting compound is found, details are worked out by specially designed experiments followed by well-designed therapeutic clinical trials. All this means hard work and expense.

##### Genius

Edison believed that there is no success without effort. Perhaps his best-known saying is his definition of genius: 'Genius is 1 per cent inspiration and 99 per cent perspiration', and he always worked according to this definition.

Science is not due solely to the genius of great men. Great men have had decisive effects on the progress of science, but no discovery of any effective kind can be made without the preparatory work of hundreds of comparatively minor and unimaginative scientists. These people accumulate the necessary data on which the great man can work.

Everyone is influenced by what he has learned from his predecessors, though his own experience, thought and experiment may enable him to advance knowledge by arriving at different conclusions from those held by his contemporaries. Many discoveries have not been dependent upon the work of especially gifted men. Yet there is even today a tendency in medicine, as in technology, to attribute progress romantically and falsely to individual genius, rather than to the efforts of thousands of persons in the past and present.

##### Students

Medical research, like most human activities, advances by virtue of contributions from many different types of individuals working at different levels. Greater recognition is therefore accorded to the 'little researcher'; and to foster this, education in modern times has at all levels been permeated with a tremendous concern for the adequate development of students, especially those who are gifted.

There is no reason why selected students should not take part in research programmes, especially in team work. Even the best

scientists require aid and, for many adventures in research, friendly cooperation is required between individuals working under strict collective discipline. In a good deal of modern research many individuals take part in an enterprise and are responsible for joint conclusions.

Reference has already been made to medical students and other young investigators whose names are now famous in medical history. But fame, or notoriety, does not depend only on brilliant discovery; for example, although he did not discover ether it was W. T. G. Morton (1819-1869), a second-year medical student at Harvard Medical School who, after numerous experiments on himself, the family dog, cats, hens, and rats, used ether to anaesthetize a patient for Dr. J. C. Warren, Professor of Surgery at Harvard, in a public demonstration of 16 October 1846. When the patient was anaesthetized, Morton said those memorable words that have echoed through the years: 'Dr. Warren, your patient is ready,' and at the end of the operation Warren turned to his audience and said: 'Gentlemen, this is no humbug'.

In training students, teachers must constantly bear in mind that their subjects are so vast that the student is apt to become lost in a maze of factual knowledge if he is not provided with adequate guidance. Students must not only be instructed, but also guided and inspired. Prof. Noah Morris considered the teacher had failed if, at the end of his discourse, he was not mentally exhilarated and physically exhausted. The good teacher is forced to recognize the inevitable gaps in his own knowledge and understanding. As a good teacher he will stimulate his students to investigate these gaps.

We have to recognize that we are all ignorant about many matters, even in the common diseases with which doctors have to deal. Older men in control of research must be careful not to dominate or to dictate to younger men working with them. They must also not be isolated, aloof and inaccessible. They should be readily approachable as advisers.

We are all students and there is no sharp line of demarcation between us. Young people also have ideas, but this is not enough. Storm van Leeuwen said that he was weary of young men who could produce brilliant ideas; he was only interested in young men who were so troubled by a brilliant idea that they could not rest until they had demonstrated by experiment how true the idea was.<sup>6</sup> This admonition has general application as well as specific application to undergraduate students.

Research need not be confined to the laboratory. Many great discoveries in medicine have been made at the bedside by those rare individuals with the ability not only to see, but also to seek an explanation of a phenomenon which they and others have observed repeatedly in their patients.

##### Conditions

Certain conditions must be fulfilled if the advancement of science is to be encouraged to flourish and grow.<sup>3</sup>

1. The first condition is that the material support of scientific research should be on an adequate scale. Progress is halted by the lack of suitable materials and funds.

2. The individual scientific worker should get the conditions, opportunities, and incentives that will enable him to give his best service.

3. The basic condition for research to flourish is the human one. There is no real shortage of intellectual ability in the human race. The achievements already made have been the work of a handful of men, but by calling on men and women of all classes and peoples, the rate of advance of science should multiply manifold. University education must be made available to large numbers. A scientific education will provide the field from which will come the research workers who will build the science of the future.

4. Individuals do not do their best work alone. The best results occur when a number of people work together. Through mutual suggestion and emulation the chance of hitting on significant discoveries is enormously increased.

#### CONCLUSION

We are living in a stirring scientific era, and to be young in mind and spirit, even if not in years, is important if we are to participate in the interesting and exciting developments of our time. All of us who are privileged to be students must improve our knowledge and retain youthful enthusiasm for new discoveries. By being thus



equipped we too may be able to assist others to make, or to make ourselves, a contribution to medical science.

This paper is published with the permission of the Medical Students' Council, University of Cape Town, under whose auspices the Memorial Address was given.

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## FIBRINOLYSIS IN RELATION TO LIPAEMIA AND INTRAVENOUS HEPARIN IN THE WHITE AND BANTU\*

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Fibrinolytic activity was studied in 22 White and 20 Bantu subjects using the 1:10 blood clot lysis time (BLT) of Fearnley *et al.*<sup>1</sup> as modified by Lackner and Goosen,<sup>2</sup> as well as the euglobulin lysis time (ELT) described by Von Kaula and Schultz.<sup>3</sup> Subjects were tested fasting and 3 and 4 hours after breakfast.

Variations in fibrinolysis which occur 3 and 4 hours after the ingestion of 70 G. of butter fat were found to be identical with those occurring after a fat-free breakfast. It was therefore concluded that lipaemia did not appreciably affect fibrinolysis.

Spontaneous acceleration of fibrinolysis over the 4-hour period of observation was found to be statistically significant with respect to BLT in the Whites (difference from fasting sample being 5.1 hours), but not in the Bantu (difference from fasting sample 1 hour). With respect to ELT, statistically significant acceleration occurred in both Whites and Bantu, but was found to be twice as great in the Whites, i.e. 0.8 hours as opposed to 0.4 hours.

As a result of the diurnal variation manifested by the Whites, their mean lysis time tended to approach that of the Bantu during the course of the morning. However, this diurnal variation was unable to abolish the statistically significant difference in fibrinolytic activity between Whites and Bantu, which has previously been reported by us.<sup>4</sup>

Since it is well known that heparin has a marked fat-clearing effect on lipaemic plasma, it was decided to test the effect on fibrinolysis of heparin given at the height of lipaemia. Accordingly 9 White and 9 Bantu subjects were given an injection of 75 mg. of heparin (10,000 units) in a volume of 2 ml. 3 hours after the ingestion of 70 G.

of butter fat. Blood was taken immediately before and 1 hour after the injection, and the fibrinolytic activity of the 2 samples was compared. As a control the experiment was repeated on another day under identical conditions, but instead of heparin, 2 ml. of saline were given. Again the fibrinolytic activity of the blood sample taken immediately before and 1 hour after the injection was compared.

It was found that heparin significantly accelerated fibrinolysis as measured by BLT in Whites (acceleration 3.6 hours,  $p = 1\%$ ) and Bantu (acceleration 2.2 hours,  $p = 2\%$ ). As measured by ELT, the acceleration in the White subjects (0.5 hours) and in the Bantu (0.3 hours) was statistically significant at the 5% and 2% levels respectively. The effect of saline was variable and not statistically significant. On comparing the changes in fibrinolysis occurring on the heparin day with those occurring on the saline day, it was found that they were statistically significant only with respect to BLT. They failed to reach statistical significance with respect to ELT partly because of paucity of numbers and partly because the heparin effect appears to be more marked with BLT than with ELT.

The fibrinolysis-accelerating effect of intravenous heparin, previously shown by us to be present in fat-free plasma,<sup>5</sup> has now been demonstrated in lipaemic plasma. The exact mechanism is obscure, but we do not feel that it is due to the actual removal of chylomicrons from the plasma.

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## PAPERS: MEDICAL CONGRESS

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THE SUPERIORITY OF METHOHEXITAL OVER THIOPENTONE

Can it be that our old friend thiopentone, synonymous with intravenous anaesthesia for a quarter of a century, and successful in surviving the synthesis of over two thousand 'ultra-short-acting' barbiturates in the attempt to find a truly short-acting anaesthetic, is at last to be superseded by the newcomer, methohexital ('brietal', 'brevital')? For it has now been established, in thousands of patients and under adequately controlled conditions in some of the best research institutions in the world, that if 2½% of thiopentone or 1% of methohexital (alternatively 5% of thiopentone or 2% of methohexital) is used for induction of anaesthesia, and nitrous oxide is then added for a standard operation, and if both barbiturates are injected at the same rate, the degree of anaesthesia obtained and its quality on the average are quite similar, except that awakening following methohexital is approximately twice as rapid and orientation is faster and more complete than with thiopentone. In South Africa, with its lack of good recovery-room facilities, these are indeed significant factors. An undeniable corollary is that thiopentone should not be used at all any longer in ambulant patients, such as those undergoing minor dental procedures.

Claims like the above were made unjustifiably for so many predecessors of methohexital, notably for buthalitone, methitural, and even the steroid hydroxydione ('viadril', and later 'presuren'), that one has become inclined to suspend judgment on initial claims as in the case of 'improvements' on morphine. Moreover, thiopentone is so firmly entrenched in modern anaesthesia that patients ask for it by name, and hospital administrators order it in bulk without any qualms. There is however nothing at all sacrosanct about thiopentone. On the contrary, Keating<sup>1</sup> noted in 1956 that intravenous anaesthetics cause as many sudden unexplained deaths as did chloroform, and Dobkin and Wyant<sup>2</sup> list extensive reviews from which it is clear that the estimated death rates from intravenous anaesthetics have been conservative. The administration of thiopentone and hexobarbitone to casualties at Pearl Harbour in 1941 was described as 'an ideal form of euthanasia'.<sup>3</sup> But even if overdosage is avoided in the shocked patient, who is exquisitely sensitive to thiopentone, a number of research workers<sup>4-6</sup> beautifully illustrated the sudden deterioration of the compensatory circulatory mechanisms and the relatively poor adjustment to sudden blood loss which is characteristic of thiopentone anaes-

thesia. Howland and Papper<sup>7</sup> noted the particularly hazardous properties of thiopentone in neurosurgical conditions; and in obstetrics, thiopentone passes readily from the maternal blood stream into the foetus, intoxicating those who are premature or at all depressed.<sup>8</sup>

Weyl *et al.*,<sup>9</sup> as well as Barron and Dundee,<sup>10</sup> found that methohexital lacks the depressant effect of thiopentone on the cardiovascular system, while Green and Jolly<sup>11</sup> found it ideal for ambulant dental patients.

The local irritant action of methohexital is unquestionably less severe than that of equipotent concentrations of thiopentone; on the other hand some authors were impressed by a higher incidence of excitatory phenomena, although these were readily controlled by either nitrous oxide or premedication with an opiate. This latter observation is of great interest in that it favours Claude Bernard's view of a century ago, supporting the idea of an opiate for pre-anaesthetic medication, rather than Beecher's view, according to which a barbiturate is safer and more rational.<sup>12</sup>

The greatest champion of thiopentone through the years, John Dundee, has just published a review (in collaboration with Barron<sup>10</sup>) in which they confirm the findings (discussed above) of leading research workers elsewhere, notably of Eckenhoff in the United States and Wyant in Canada. We nevertheless look forward to publication of results from a South African author, since methohexital has been under investigation at all the main university hospitals in South Africa for some time.

Unlike halothane, which is in essence a fluorinated chloroform with all the dangers of great potency and with only a slightly better therapeutic index, all anaesthetists in South Africa, whatever their status, will be pleased to add this new and truly 'ultra-short-acting' oxybarbiturate, methohexital, to the repertoire.

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DIE KONGRESPROGRAM

Die algemene, tweejaarlikse, mediese kongres wat gedurende die week 24 - 30 September in Kaapstad gehou word, is die voortsetting van 'n lang en trotse tradisie in die geskiedenis van ons mediese beroeps- en akademiese lewe in Suid-Afrika. Deur al die jare heen is hierdie tradisie volgehou, en aan daadwerklike en entoesiastiese ondersteuning van die kant van die lede van die Mediese Vereniging was daar nooit gebrek nie.

In sekere opsigte het ons omstandighede wat betref die hou van kongresse egter verander. Binne die raamwerk van die Mediese Vereniging het daar gedurende die afgelope paar jaar 'n groot aantal gespesialiseerde groepe ontstaan.

Hierdie groepe funksioneer as nasionale groepe binne die Vereniging, en hulle maak dit dus moontlik vir sulke groepe soos die chirurgie, interniste, pediater, ginekoloog en obstetrici, hospitaal-administrateurs, algemene praktisyns, ens. om hul eie groepsbelange te behartig. Afgesien van die praktiese en professionele aspekte van hul werk, wat lede van die groepe met mekaar bespreek, hou hulle gereeld groepskongresse. Na die groepskongresse kom dan die lede van die groep, en hulle nooi dikwels vooraanstaande geneesheren uit ander lande om aan hul kongresse deel te neem. Sommige van hierdie groepskongresse het in die verlede al 'n besondere hoë standaard bereik, soos ook wel blyk uit

die gepubliseerde werk van lede van die groepe wat van tyd tot tyd in spesiale uitgawes van die *Tydskrif* geplaas word.

Die vraag ontstaan of daar nog plek vir 'n tweejaarlikse *algemene mediese kongres* is. Laat ons dadelik sê dat ons aan die antwoord op hierdie vraag hoegenaamd geen twyfel het nie. Daar bestaan nog altyd 'n dringende behoefte aan so 'n kongres. Die algemene kongres skep die geleentheid vir die breë lae van die mediese professie om nog as 'n *eenheid* op te tree. In 'n tyd van versplintering en in 'n tyd waar spesialisasie en die algemene praktyk dreig om middelpuntvlindende kragte te word, verteenwoordig so 'n kongres 'n eenheidsbeginsel en 'n saambindende faktor. Die betekenis van die kongres in hierdie verband kan nie oorskat word nie.

Daarby bied die kongres die geleentheid vir algemene besprekings oor onderwerpe waarin lede van alle groepe belang stel. Die onderwerpe vir die voltallige sittings is 'Diabetes' en 'Die Versorging van Bejaardes'—onderwerpe wat daarop bereken is om die belangstelling van alle geneesher te prikkel. Daar sal by hierdie kongres ook die geleentheid wees vir uitgebreide gekombineerde samesprekings oor sulke onderwerpe soos respiratoriese versaking, antibiotiese middels, chemoterapie, kruisinfeksie, en afsluitende bloedvattoestande. Hierdie onderwerpe is van prominente belang vir lede van verskillende subgroepe. Ook is daar die geleentheid vir die nasionale groepe self om te vergader, en vir hul lede om bydraes te lewer in seksievergaderings wat net vir hulle bedoel is. Die kongres is dus in werklikheid 'n algemene kongres wat terselfdertyd voorsiening maak vir die bevrediging van die behoeftes van selfs die mees gespesialiseerde lede van die professie.

As hooggeplaaste besoekers word onder andere verwag dr. J. H. Sheldon van Wolverhampton, Engeland, wat 'n deskundige is op die gebied van die versorging van bejaardes. Hy is ook president van die Britse Geriatriese Vereniging. Prof. M. Rachinilewitz, dekaan van die Fakulteit van Geneeskunde van die Hebreeuse Universiteit, Jerusalem, sal ook teenwoordig wees en deelneem aan die kongres. Die formele opening van die kongres sal deur die eerste President van die Republiek van Suid-Afrika waargeneem word.

By die kongres sal daar ook 'n wetenskaplike uitstalling wees. Hierdie onderneming staan onder die leiding van dr. H. O. Hofmeyr, en die vooruitsigte is dat dit 'n besonderse hoë gehalte sal wees. Daar sal verder 'n uitstalling van stokperdjies wees, 'n mediese en chirurgiese uitstalling, en 'n omvattende uitstalling van farmaseutiese produkte en mediese instrumente en apparaat. Reëlins word getref vir uitvoerige beeldradio-uitsendings van verskillende soorte operasies. En Kaapstad sal sorg dat sy tradisie van gasvryheid weer tot sy reg kom—daar sal 'n kongresbal wees, 'n banket, 'n burgemeesterlike onthaal, geleentheid vir deelname aan allerhande sportsoorte, uitstappies, en spesiale onthale vir die vrouens en ander familieleden van dokters wat die kongres bywoon.

In hierdie tye van spanning en drukte wat deursypel tot haas alle vlakke van ons lewe, verteenwoordig 'n kongres soos hierdie dié soort menswaardige aktiwiteit wat in sy wesenlike aard positief en opbouend is. Die wêreld het behoefte aan hierdie soort aktiwiteit. Laat ons die geleentheid om deel te hê aan sulke skeppende optrede met gewillige hande en warm harte aangryp.

#### AUDIO-DIGEST FOUNDATION TAPE-RECORDING SERVICE

On 25 March 1959 Dr. F. A. van Heerden of Bergville, Natal, wrote (in a letter to the Editor): 'It would appear to be an established practice in the USA to have interesting medical lectures recorded on tape and to make the tapes available, for a small consideration, to members of the medical profession. This procedure would be of great value to those of us who live in the country and who cannot enjoy the privilege, as our city colleagues do, of attending lectures by some of our learned teachers or of well-known visitors from other lands. Perhaps you would consider ways and means of instituting a similar service in this country'.

Since the publication of Dr. van Heerden's letter, two interesting developments took place. Firstly, the Cape of Good Hope Faculty of the College of General Practitioners was established. Among many other important services rendered by this Faculty, they now run a tape-recording service for members of the College. The firm Smith Kline and French Laboratories has kindly and generously assisted the College in making this service possible.

Secondly, the firm Squibb Laboratories introduced a unique service to members of the medical profession in South Africa by making available on free loan for individual or group listening, tape-recorded reviews of current medical literature and scientific lectures prepared by the Audio-Digest Foundation, a non-profit making subsidiary of the

California Medical Association. Squibb Laboratories subsequently made the generous donation of the whole of their recorded Tape Library to the Medical Association on the understanding that the Association would be willing to continue the service. The Medical Association have now become subscribers to the Audio-Digest Foundation Tape-recording Service.

These recordings cover a wide field of interest to all members of the medical profession and medical students, and include, amongst recordings by guest lecturers, some by the leading men of medicine and surgery in the United States of America. The five-inch reels of tape provide about 1 hour of the most interesting and enjoyable listening to a well-chosen selection of expertly summarized articles from the world medical literature. Not only are the articles read with the clarity and resonance of an expert reader, but they also include experts summing up important points in their own special fields.

The tapes are received at regular weekly intervals, and the new releases as well as back numbers from the existing Tape Library are available on free loan from the Association. Further information about the subjects and series which are available, as well as any other information in this connection, is obtainable from The Business Manager, Medical Association of South Africa, P.O. Box 643, Cape Town.

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## AORTO-ILIAC OCCLUSIVE DISEASE\*

## A REPORT ON 67 CONSECUTIVE CASES TREATED SURGICALLY

J. H. LOUW, CH.M. (CAPE TOWN), F.R.C.S. (ENG.) and W. M. ROBERTS, M.MED. (SURG.) (CAPE TOWN), F.R.C.S. (ENG.)

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(Continued from page 350 of the Journal for 29 April 1961)

## SYMPTOMS AND SIGNS

## Intermittent Claudication

Intermittent claudication was the outstanding symptom. It was present in every case and the first symptom in 64 (95%).

The term is derived from the Latin *claudicare*, to limp or halt,<sup>10</sup> and is usually defined as a discomfort of varying severity produced by exercising a muscle under ischaemic conditions, and rapidly relieved by rest.<sup>22</sup> (It was first described by the veterinary surgeon Boullay in 1831, who observed it in a six-year-old mare suffering from obliteration of her femoral arteries — when she trotted the blood-supply was insufficient and the result was '*une douleur profonde*'. The clinical picture was clearly described by Charcot in 1858.<sup>23</sup>) It is due to the fact that, when the circulation to a muscle is impaired, repeated activity causes it to outstrip its blood supply.

Unfortunately intermittent claudication has become synonymous with pain in the calf on walking and therefore variations, which are common, are often not recognized.<sup>4,11,14</sup> In the first place the symptom need not be a severe pain which is alarming to the patient. It may be a dull ache, a cramp or a burning sensation; it may simply be a discomfort, a tightness, a weakness or a feeling of profound fatigue; some patients describe it as a feeling 'as if the limb does not belong' to them. In aorto-iliac disease in particular a common complaint is 'an extreme weariness' first described by Leriche.<sup>18</sup>

In the second place, it may be located in any muscle which has its blood supply impaired during exercise. The intermittent claudication of aorto-iliac disease may occur in the back, hip or buttock, thigh or lower abdomen.<sup>2,4,11,14,24</sup> This may occur alone or in association with

calf claudication, but when there is associated occlusion of the femoral or distal vessels, calf claudication often dominates the picture. The areas affected in our patients are shown in Fig. 6 and the clinical patterns are given in Table III. The following observations are of interest:

1. The outstanding symptom was pain or distress in the hips and/or thighs, particularly in patients with localized occlusions (86%).

2. Symptoms occurred at a high level (back, hip, thigh, abdomen) in 25 (89%) of the 28 patients with localized occlusions and in 44 (66%) of the series as a whole. On the other hand 60 (90%) of the patients had symptoms

TABLE III. CLAUDICATION PATTERNS

	A	AI	I	IF	AIF	Total	Remarks
Number of patients	7	15	6	6	33	67	
Back, hip and thigh	—	2	—	—	—	2	} Proximal to calves only
Thigh and/or hip	—	2	—	—	3	5	
Back, hip, thigh, calf	1	1	—	—	4	6	
Back and calf	—	1	—	—	1	2	
Hip, thigh and calf	4	4	2	1	4	15	Hypogastric pain in 1
Hip and calf	1	2	1	2	1	7	Hypogastric pain in 2
Thigh and calf	1	2	1	—	3	7	
Feet and/or calf	—	1	2	3	17	23	Femoral involved in 20 (87%)

Arteries involved: back—aorta, hip—aorta or common iliac, thigh—external iliac, hypogastric—internal iliac, and calf—femoral or external iliac.

Grades of claudication: grade 1, 3; grade 2, 11; grade 3, 53.

A—aortic bifurcation, AI—aortic bifurcation + common iliacs, I=iliac vessels (common, internal or external iliac), IF=iliac + common and superficial femoral, and AIF=aortic bifurcation + iliac + femoral.

referable to the calves. De Wolfe *et al.*<sup>11</sup> found that 55.3% of their patients with localized occlusions had no symptoms below the knees, but this was so in only 4 (14%) of our 28 cases with similar lesions.

3. In 23 (34%) of the patients distress was limited to the calves. However, 20 of these had associated femoral occlusions. Of the 28 with localized occlusions only 3 (10%) had symptoms in the calves alone.

4. There was associated backache in 10 cases (15%) and lower abdominal pain in 3 (4%). Others<sup>14</sup> have reported cases where low back pain was the initial and major symptom.

5. It may be concluded that aorto-iliac occlusion usually gives symptoms referred to the region of the hips and thighs with radiation to the calves. This is occasionally accompanied by backache and rarely by abdominal discomfort.

In the early stages the distress would involve only 1 limb or group of muscles and would come on only after violent exercise or walking long distances. Gradually other muscle groups and the opposite limb would become involved and the claudication distance would become progressively less. At first the patient would find that the symptoms subsided with further exercise (grade 1—3 cases); later there would be no relief but they could still force themselves to carry on (grade 2—11 cases); finally

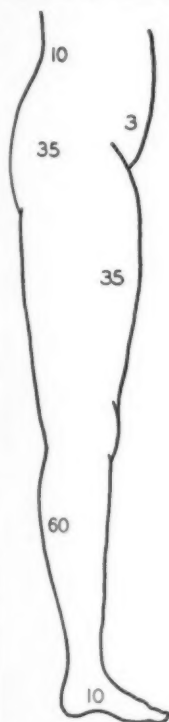


Fig. 6. Sites of claudication.

\* Paper presented at the Annual Congress of the South African Orthopaedic Association (M.A.S.A.), Cape Town, 13 October 1960.



the distress would become so intense that they found it impossible to continue walking (grade 3—53 cases). Eventually the walking distance might be reduced to 10–15 yards (the effort of standing upright might even be sufficient to produce the distress), and the time of rest required for the distress to abate would become progressively longer. At this stage there were also other symptoms and signs of ischaemia.

#### Rest Pain (Table IV)

Rest pain was present in only 18 (27%) patients and 14 of these had involvement of the femoral vessels. This is in keeping with the objective findings mentioned below.

#### Major Ischaemic Effects (Table IV)

Major sequelae of ischaemia such as sensory disturbances, trophic changes, ulceration and gangrene were uncommon and occurred in about a quarter of the

TABLE IV. CLINICAL FEATURES—LOCAL

Features	Subjective (Patients—67)	Objective (Limbs—129)	Remarks
Claudication	67	—	Only proximal to calves in 7 (10.5%)
Rest pain*	18	—	Femoral involved in 14 (78%)
Sensory disturbances*	27	19	Femoral involved in 16 limbs (84%)
Trophic changes*	13	17	Femoral involved in 14 limbs (82%)
Ulcers and gangrene*	10	10	Femoral involved in 9 limbs (90%)
Colour changes	20	46	Pallor in 16 limbs, cyanosis/rubor in 30 limbs
Positive Goldflam's sign	—	62	
Coldness	36	58	
Wasting	—	34	
Impotence	13	—	Internal iliacs involved in all

\* Four out of 5 patients with rest pain and ischaemic changes had femoral involvement.

patients. Of these, 4 out of 5 had femoral involvement. This was pointed out by Leriche<sup>18</sup> and has been confirmed by all subsequent reports.<sup>9,11,14,29</sup> Ulceration and gangrene were particularly rare (10 patients) and occurred in only 1 of the patients with localized disease. In this patient an indolent ulcer followed trauma to the leg and was in fact the first symptom. In this connection it is of interest that Leriche<sup>18</sup> warned that 'if an incision is made in the limb the wound heals very sluggishly or not at all'. It is this absence of major ischaemic effects that has led to many mistakes in diagnosis for, as Leriche<sup>18</sup> points out, 'it is difficult to believe that the circulation is impaired'. Further confusion may arise in those rare cases where ischaemia of the spinal cord may result in alteration of the tendon jerks and other signs suggestive of orthopaedic disorders.

#### Coldness (Table IV)

Coldness, both subjective and objective, occurred in about 50% of patients irrespective of the type of occlusion. It should be regarded as an important feature and was the first symptom in 2 patients. In some patients it was associated with Raynaud's phenomenon in winter or when the feet were immersed in cold water.

#### Colour Changes (Table IV)

Colour changes were noted in about a third of the patients. Cyanosis or rubor was twice as common as pallor which, however, has been stressed by Leriche and others as an important feature of aorto-iliac occlusion. Only

rarely did we see the striking pallor giving the skin the ivory or marble-like appearance, with thin blue veins, described by Leriche. This is in keeping with the findings of de Wolfe. On the other hand, Goldflam's test was positive in 50% and in these patients extreme pallor was noted during the test. It is generally agreed that this test is of value and will show a positive result when the earliest symptom of claudication appears.<sup>18</sup>

#### Wasting (Table IV)

Muscular wasting was noted in about one-third of the patients and these complained especially of loss of power or fatigue on exercise. Leriche found 'global' atrophy to be common, but mentions that it may be difficult to appreciate because both limbs are affected. Others have also commented on wasting which may at times be extreme.<sup>9</sup> Certainly some of these limbs looked as if they were made of skin and bone only. Lesser degrees of wasting may be missed because of the lack of a normal limb for comparison.

#### Impotence (Table IV)

Leriche laid great stress on impotence in the male, referring to the symptom as an 'inability to keep a stable erection, the blood flow being insufficient to fill the spongiosus processes'. He continued that 'if the disease is left to itself, sexual impotency will soon be permanent' and pointed out that 'genital troubles are more noticeable (in patients who are still young) since they appear in full youth'. The accuracy of Leriche's description should be noted—the symptom is not 'loss of libido' as is sometimes stated.<sup>29</sup>

The symptom was present in 13 (30%) of our male patients, and a similar incidence has been found in other series.<sup>9,29</sup> All of them had bilateral disease involving the common and internal iliac vessels, which supports the presumption that the symptom is due to impairment of the blood supply to the corpora cavernosa through the internal pudendal artery.<sup>29</sup> None of the patients had evidence of 'spinal-cord claudication', bladder dysfunction or testicular atrophy.

#### Pulses (Table V)

Aortic pulsation above the umbilicus could be felt in all the patients. The presence of a bruit over the terminal aorta was recorded in 10 patients, but the actual number

TABLE V. PERIPHERAL PULSES

	A	AI	I	IF	AIF	Total
Number of cases	7	15	6	6	33	67
Aortic bruit	—	6	—	—	4	10
Number of limbs:						
iliac	14	30	8	11	66	129
femoral	—	—	—	8	55	63
Femoral pulses:						
present	9	22 (br. in 9)	5	9 (br. in 4)	42 (br. in 13)	87
absent	5	8	3	2	24	42
Popliteal pulses:						
present	6	13	3	3 (br. in 3)	11	36
absent	8	17	5	8	55	93
Pedal pulses:						
normal	4	9	4	—	5	22
diminished	2	9	1	1	7	20
absent	8	12	3	10	54	87

\* Limbs without femoral involvement—66, pedal pulses in 42 (64%); limbs with femoral involvement—63, pedal pulses in nil.  
A, AI, I, IF, AIF as in Table III; br.—bruit.

was probably greater because this sign was not always carefully looked for, especially in the earlier cases.

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Femoral pulses were present in two-thirds of the limbs, but were often weak and tended to disappear with exercise. Bruits were recorded in 26 (20%), but unfortunately, the vessels were not auscultated after exercise. Popliteal pulses were present in 36 (28%) of the limbs and bruits were recorded in 3.

Pedal pulses were present in 42 (33%) of the limbs, but in half of these they were diminished, i.e. they were either of poor volume or 2 of the 3 pedal pulses (dorsalis pedis, posterior tibial, perforating peroneal) were absent or they disappeared on exercise. Significantly, pedal pulses were present in 64% of the limbs without femoral occlusion and in none of those with femoral occlusion.

The presence of pulses in so many of our patients is in keeping with the rarity of rest pain and major ischaemic changes. It is a feature which, although recorded in reported case histories, is not stressed in the literature.<sup>6,11</sup> Leriche<sup>10</sup> stated that 'no pulse can be found, either in the leg or in the groin'. It is therefore important to emphasize that both groin and pedal pulses may be present in complete occlusions of the aorta and iliac arteries. It should be mentioned, however, that the pulses tend to disappear on exercise<sup>1</sup> and if the patient is examined soon after a period of activity, no pulses may be felt.

#### Associated Cardiovascular Disease (Table VI)

There was evidence of associated cardiovascular disease (excluding hypertension) in 38 (58%) of the patients, particularly among those who had diffuse disease. A high incidence has also been reported by others,<sup>8,9,28,29</sup> and the common associated lesion is coronary heart disease. This is a factor which obviously affects prognosis and it should be noted that 6 of our patients developed postoperative coronary thrombosis.

Carotid bruits were recorded in only 10 patients. Although there were no histories of carotid insufficiency, this figure is probably low because the carotid vessels

TABLE VI. ASSOCIATED CARDIOVASCULAR DISEASE

	A	AI	I	IF	AIF	Total
Number of patients	7	15	6	6	33	67
Number with cardiovascular disease	3	8	2	5	20	38
History:						
Coronary	—	3	1	—	4	8
Angina	—	—	—	—	2	2
Failure	—	2	—	2	6	10
Stroke	—	—	1	1	1	3
Thrombo-embolism	1	—	1	1	1	4
Examination:						
Cardiac signs	—	2	1	—	5	8
Carotid bruit	—	1	—	3	6	10
Special:						
Abnormal ECG	1	5	1	2	12	21
Retinopathy	—	—	—	—	4	4
Albuminuria	—	—	—	—	3	3
Postoperative:						
Coronary	1	2	—	2	1	6
Renal failure	—	—	—	—	1	1

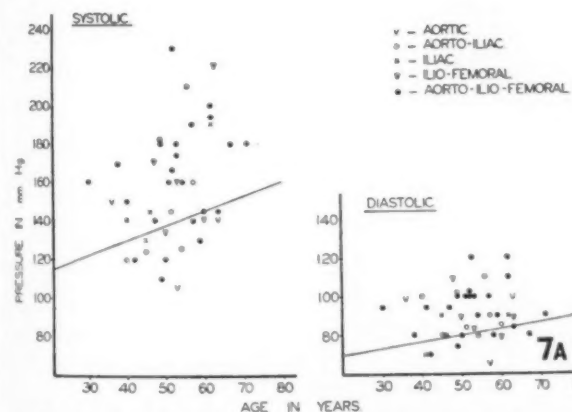
A, AI, I, IF, AIF as in Table III.

were not always auscultated, particularly in the earlier cases, and recently we have found that bruits are often present. In none of the patients in this series was there obvious evidence of involvement of the brachio-cephalic trunks. More recently, however, we have treated 3 women, aged 28, 29 and 40 years, suffering from diffuse aorto-ilio-femoral disease, who also had involvement of the aortic arch with stenosis of the common carotids and subclavian arteries.

None of the patients in the series had obvious involvement of the renal or superior mesenteric vessels, but in one of the patients mentioned above there was stenosis of the origin of the left renal artery due to an atheromatous plaque. Furthermore, in another patient in the series there was severe postoperative oliguria with renal failure which might have been due to renal-artery obstruction.

It has been stated that thrombophlebitis and pulmonary embolism are frequently associated with aorto-iliac disease.<sup>28</sup> Four of our patients gave a history of thrombo-embolism. In 2 it followed on prolonged bed rest for

#### BLOOD PRESSURE - MALES



#### BLOOD PRESSURE - FEMALES

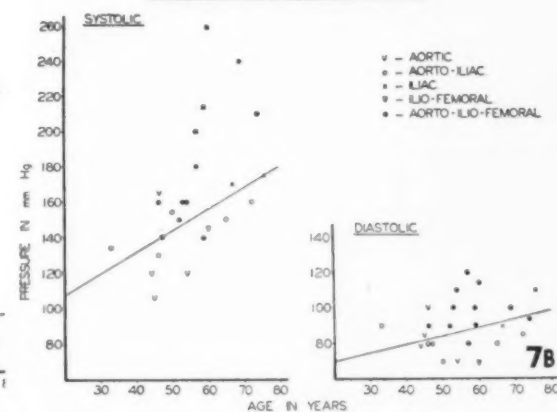


Fig. 7A and B. Scattergrams showing levels of blood pressure plotted in relation to the mean normal for age and sex (Pickering<sup>21</sup>).

coronary thrombosis, in 1 it followed a previous lumbar sympathectomy, and in the fourth it occurred spontaneously. In none of them was there any recurrence. None of our patients suffered from superficial phlebitis although varicose veins were common. It should also be noted that only 10 of the patients had haemoglobin levels above 16 G. per 100 ml. and that none were anaemic.

#### Blood Pressure (Figs. 7A and 7B)

Hypertension was not particularly common in the series as a whole. The diastolic pressure was below 90 mm.Hg in 23; from 90 to 100 in 20; from 100 to 110 in 14; from 110 to 120 in 6, and above 120 in 4. However, there was a tendency for both systolic and diastolic pressures to be raised in the males at all ages (Fig. 7A).

In both males and females with diffuse aorto-ilio-femoral disease, hypertension was common. In this group the diastolic pressure was below 90 mm.Hg in 6; from 90 to 100 in 11; from 100 to 110 in 9; from 110 to 120 in 3; and above 120 in 4. Figs. 7A and 7B show that in practically all the patients both systolic and diastolic pressures were above the average for the age-group. It was in this group with diffuse disease that the aortic disease often extended up to and beyond the renal arteries and in some, at least, the hypertension might have been caused by narrowing of a renal artery from extension of the aortic thrombosis. However, none of the patients suffered from malignant hypertension, and, unfortunately, the renal arteries were often not visualized on the aortograms. (A more recent case of renal hypertension associated with diffuse aorto-ilio-femoral thrombosis has already been referred to.)

#### Serum Cholesterol (Figs. 8A and 8B)

The blood-cholesterol levels were determined in 50 patients. Figures varied from 155 to 374 and in 23 of the patients the level was above 300 mg. per 100 ml. (In a more recent case the serum cholesterol was 420 mg. per 100 ml.) From Figs. 8A and 8B it will be evident that there is a tendency for the cholesterol levels to be raised, equalling and even exceeding those in patients with coronary thrombosis. It should also be noted that only 3 patients in the series had diabetes, which is in keeping with the findings of others. Twenty-two of the patients were very obese.

It is remarkable that the cholesterol levels were particularly high in patients with localized segmental aortic or iliac occlusion, because in them the rest of the aorta and the iliac vessels were apparently normal and associated coronary heart disease uncommon. This paradox may have a bearing on the aetiology of localized lesions and is being investigated further. De Wolfe *et al.*<sup>11</sup> have also found a high incidence of abnormal lipoprotein patterns.

#### DIAGNOSIS

1. The first essential in diagnosis is to remember the possibility of aorto-iliac occlusion in the differential diagnosis of discomfort in the back, hip, thigh or leg. Arterial obstruction must be considered in every patient who presents with low back pain, either alone or in conjunction with pain in any part of the limbs—even if the appearance of the limb does not suggest that the symptoms are of vascular origin.

2. Secondly a careful history must be taken to determine the relation of the discomfort to exercise. A history of intermittent claudication is highly characteristic of vascular insufficiency and can always be elicited on careful inquiry. The pain or discomfort comes on after walking a given distance and is usually distressing enough to cause the patient to stop. It is rapidly relieved by rest, but when activity is resumed the same amount of effort constantly reproduces the same pain in the same place.<sup>11,16</sup> The walking distance may vary, however, being decreased by a rapid pace or walking uphill, and increased by walking slowly.

No condition other than arterial insufficiency exactly reproduces this sequence. It was clearly recognizable in all our patients and we have found it so reliable that we hesitate to make a diagnosis of arterial insufficiency unless it is present.

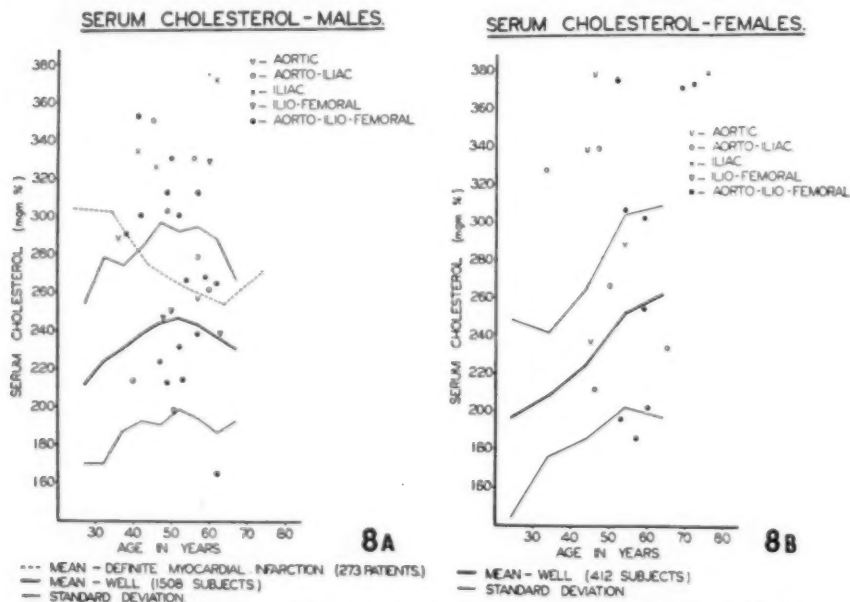
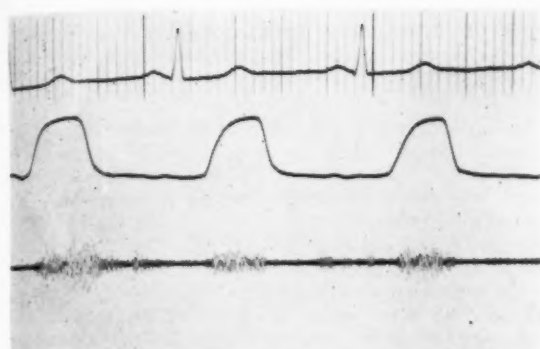


Fig. 8A and B. Scattergrams showing levels of serum cholesterol plotted in relation to the mean levels in well subjects and in patients with definite myocardial infarction (Lawry *et al.*<sup>17</sup>).

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Fig. 8A and B. Scattergrams showing levels of serum cholesterol plotted in relation to the mean levels in well subjects and in patients with definite myocardial infarction (Lawry *et al.*<sup>17</sup>).



MR. J. A. AGE 51 YEARS. 11:10:60  
AORTO-ILIO-FEMORAL OCCLUSION  
PHONOGRAPH OF FEMORAL BRUIT. 9

Fig. 9. Phonograph of femoral bruit (lowest tracing), together with electrocardiogram and recording of opposite femoral pulse.

### OSCILLOMETRY.

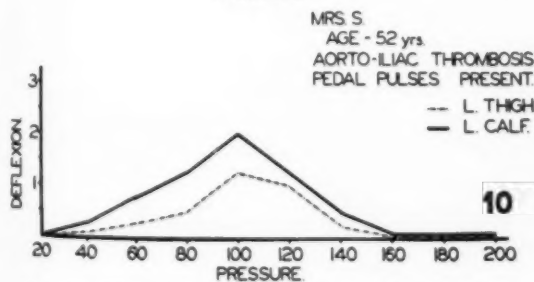
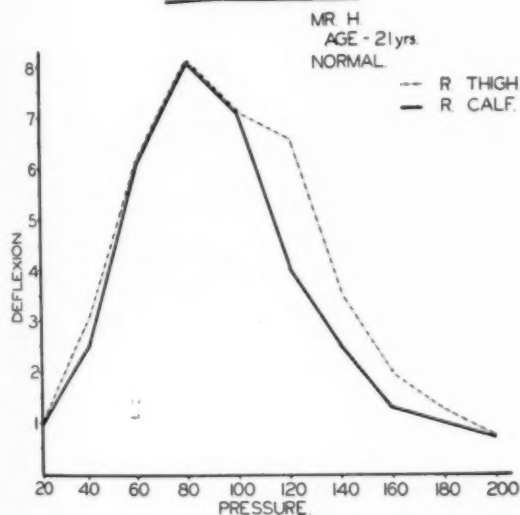


Fig. 10. Diagram of oscillometry readings indicating marked reduction in oscillation in thigh and calf of Mrs. S. (lower graph) although the pedal pulses were present. Compare with normal readings (Mr. H. — upper graph).

### OSCILLOMETRY.

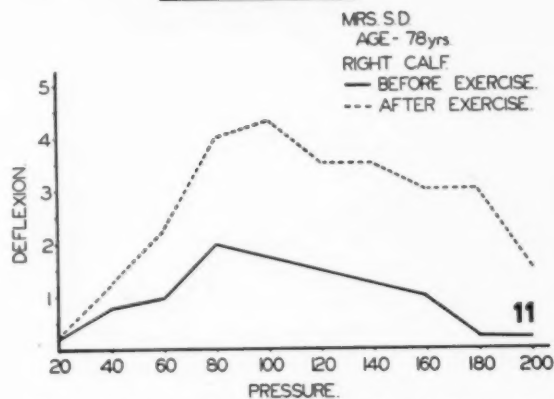
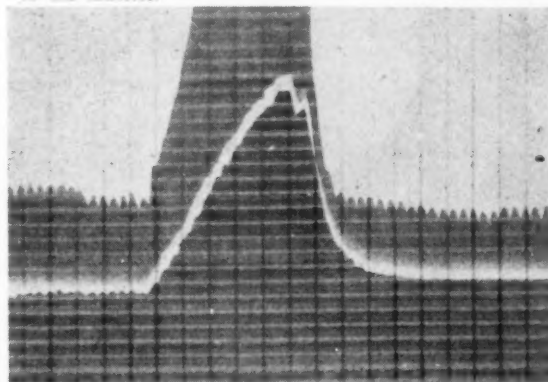
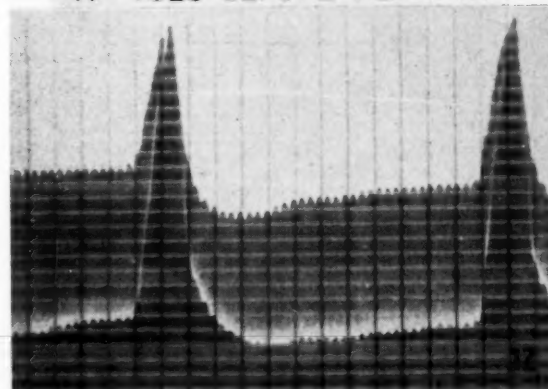


Fig. 11. Diagram of oscillometry readings indicating increased oscillation after exercise, due to shunting of blood to the muscles.



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Fig. 12. Plethysmograph showing improvement in skin circulation after reflex heating in a patient with complete occlusion of the aortic bifurcation and absent ankle pulses.

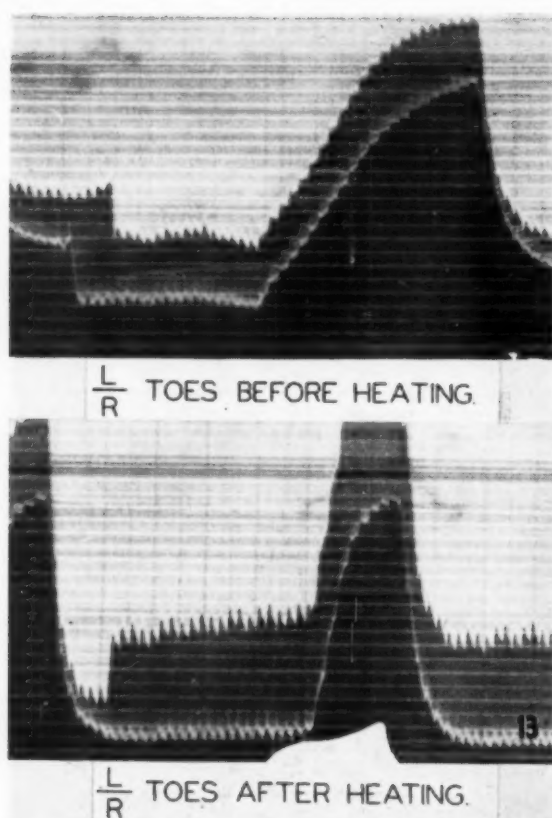


Fig. 13. Plethysmograph showing apparently good circulation although the patient had a complete block at the bifurcation of the aorta, with palpable ankle pulses. This may be misleading.

The character and distribution of the pain, on the other hand, may simulate very closely the symptoms of orthopaedic disorders.<sup>4,11,14,15</sup> Unlike the pain of prolapsed disc and other intrinsic disease of the back, however, ischaemic pain does not occur on the first movement but only after continuation of activity. Furthermore, it is not aggravated by coughing nor accompanied by an alteration in the tendon reflexes. In contrast to the pain of hip-joint disease, gluteal or thigh claudication is not associated with restriction of joint movements, nor are there areas of tenderness, trigger points or pain on passive movement usually found in fibrositis, bursitis and other soft-tissue affections which can be relieved by blocking with local anaesthetics. The same applies to the differentiation of calf and foot claudication from arthritis of the knee joint, foot strain and other bone and joint disease of the lower leg. It should be remembered, however, that a patient with arterial deficiency and exercise pains in the legs might also have osteoarthritis of his knee and hip and some metatarsalgia. He will describe his pain as an ache which came on with exercise in his whole limb, became worse throughout the day, and kept him awake at night.<sup>6</sup>

3. Thirdly, examination of the femoral and peripheral pulses should be made a routine and integral part of every orthopaedic examination. This should be done regardless of the appearance of the limbs, which are often remarkably normal.

Absence of the pedal pulses is an important sign of vascular disease, but occurs in only half to two-thirds of patients with aorto-iliac occlusion (depending on the extent of the disease). Diminished pulsation may be detected in a further sixth and these will usually show the inverse response described by Ejrup, the pulses becoming impalpable after exercise to the point of pain. In the remaining sixth the pulses will be normal although Ejrup's test may result in their diminution or disappearance. Michael Boyd<sup>7</sup> stated that disappearance of the pulse on exercise and return with rest is pathognomonic of a high arterial block.

Examination of the pulses should include auscultation of the aorta, iliac arteries and particularly the femorals before and after exercise. The presence of a bruit, which may be present only after exercise, indicates arterial stenosis and may be found in either the affected or the sound limb<sup>18,20</sup> (Fig. 9). It is of particular value in patients

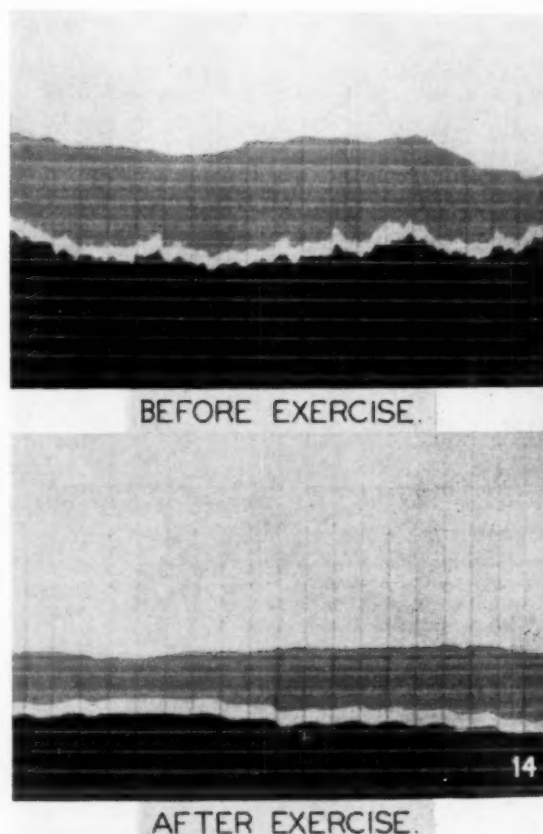


Fig. 14. Plethysmograph showing diminution of pulsation after exercise.



with palpable pedal pulses. (In complete occlusions no bruit can be heard over the artery itself but may be detected over large collaterals.)

4. Oscillometry is a valuable aid to diagnosis<sup>1</sup> particularly when the pedal pulses are present. Leriche recognized the importance of this investigation and mentioned that early 'good cases' can be detected on oscillometric examination. All our cases, including those with palpable pulses, showed reduction or absence of oscillations in the thigh and leg (Fig. 10). Furthermore oscillometry may show an increase in calf pulsations on exercise due to shunting of blood from the periphery to the muscles (Fig. 11).

5. Plethysmography is of much less value and may be misleading. In patients with severe ischaemia and absent pulses the diagnosis is obvious, and plethysmography is only of value in indicating whether the skin collaterals are capable of dilatation (Fig. 12). In others, particularly those with palpable pulses, the investigation may suggest that vascular obstruction is not the cause of the patients' symptoms (Fig. 13). Sometimes re-examination after exercise may show that the pulses disappear (Fig. 14).

6. Plain radiographs. These are of little value in the diagnosis of aorto-iliac thrombosis.<sup>11,20</sup> Aortic or iliac calcification was detected in 11 of our patients (Fig. 15). None of those with localized iliac occlusion and only 1 with localized aortic occlusion showed the presence of calcification.

Femoral calcification was present in 1 of these 11 patients and in 7 others. Among these 7 were 3 of the 6 patients with ilio-femoral occlusions and 3 patients who



Fig. 15. X-ray showing calcification of common iliac arteries.

had aorto-iliac occlusion but perfectly patent femoral vessels.

7. Aortography (Figs. 16 - 20) is the most useful investigation and was done in all but 4 of our patients. In 1 of those not investigated, aortography was deemed too risky because of extensive aortic calcification. In the other 3 the clinical diagnosis was considered definite enough to omit aortography.

We found aortography particularly valuable for the detection of the following:

(a) The exact location of the block, e.g. it differentiates between thrombosis of the lower aorta and bilateral com-

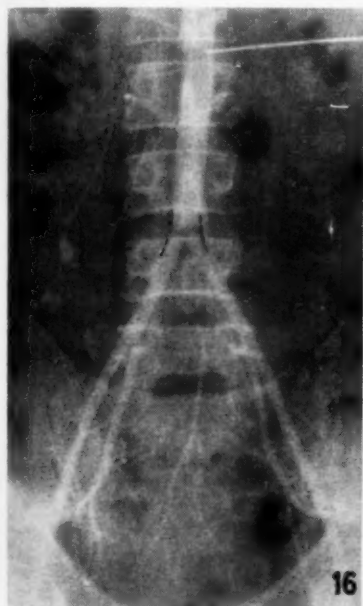


Fig. 16. Translumbar aortogram showing localized block at aortic bifurcation (compare Fig. 1A).

Fig. 17. Translumbar aortogram demonstrating complete occlusion of lower aorta, aortic bifurcation and both common iliac arteries. (Compare Fig. 1D).

Fig. 18. Translumbar aortogram showing complete occlusion of left external iliac artery. (Compare Fig. 1B).



Fig. 19. Translumbal aortogram demonstrating multiple occlusions of aortic bifurcation, iliac arteries and both femoral (Compare Fig. 1C). Note: horizontal white band represents break in continuity of thighs.  
 Fig. 20. Translumbal aortogram demonstrating multiple occlusions of the iliac arteries and both femoral arteries and profunda femoris arteries. (Compare Fig. 1E).

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mon iliac thrombosis and indicates the extent of the disease.

(b) Involvement of the renal arteries.

(c) Additional blocks in the femoral and distal leg vessels which are of great importance in assessing the 'run off' and hence the treatment and prognosis.

(d) The extent of collateral vessels, which will be discussed in another publication.

We are fully aware that the investigation is not without

its dangers and that it should not be lightly undertaken by 'occasional dabblers',<sup>29</sup> but we have been fortunate in that none of the patients in this series suffered any complications. We therefore feel justified in continuing with aortography. If symptoms are so mild that operation is not indicated, then an aortogram is not advised since it is felt that aortography is an aid in planning the extent of surgery, not in deciding whether it is indicated.<sup>30</sup>

(To be continued)

## A POSITIVE APPROACH\*

H. PENN, President, Southern Transvaal Branch (M.A.S.A.) 1960

In a developing world it is natural to expect that each year should show an improvement on the previous year. However, when assessing 1960 in its general and local contexts, it is difficult to know whether we are advancing or going backwards; whether we are heading for Utopia or dissolution. This seems to be the situation in considering the problem in both its broad and narrow aspects.

In the matter of world affairs there have been, as usual, amazing discoveries, particularly in the scientific field. In the moral field, however, there seems to be a continuous deterioration, and even the United Nations has left no doubt in the mind of most people that material advantage is considered all-important, and that moral values by themselves are of little consequence. In short, there seems to have been great technological improvements in both rockets and rackets.



Dr. Penn

In that august body, the United Nations, the World Health Organization has emerged with the cleanest record, and there is no doubt that medicine and the allied professions throughout the world can be very proud of their achievements; but, even here, the benefits to mankind are often subservient to the dogmas and prejudices of various sections of the world's community.

One of the most serious problems confronting us today is the population explosion indicated very clearly by people such as Sir Julian Huxley and Lord Bertrand Russell, who have warned repeatedly that unless cognisance is taken of this fact, over-population will reduce the world to a state which will create conflict and misery; and

that if measures for reduction in the world's populations are not urgently taken by physiological and scientific means, only violence and chaos will result in the effort to secure a place in the sun. Whilst on the one hand the World Health Organization is compelled to disregard methods of birth control because of religious principles, it is found on the other hand that, because of the improvement in hygienic methods in the backward countries (so freely made available by the Western world), the maternity and infantile mortality rates have been reduced to a minimum.

The populations of these areas are increasing, and the general mortality is being reduced by virtue of the cure of innumerable illnesses that operated in the past as the 'normal' method of population control. Moreover, with the improvement of nutrition, the expectancy of life is becoming longer and will probably, within the next few years, be doubled.

This achievement on the part of the World Health Organization is admirable, but we must also be realistic and appreciate the fact that, in the Western world, families have to decrease their numbers in order to exist at all and to provide funds for the assistance of the other side of the world where families are increasing. Therefore, whereas we of the Western world have an average of two or three

children, we support families of twenty or more in Indonesia or other places because they cannot support themselves. As medical men we must realize that we have not only a short-term duty to the sick who are living today, but also a long-term responsibility to those who are yet unborn.

But in world affairs generally, no continent has loomed larger in focus, if not in importance, than Africa. 1960 has been described as Africa's year of destiny, and we are told that things can never be the same again anywhere on the African continent after the events of this past year. As Dr. de Kiewiet, the historian, has said: 'South Africa must reconcile itself to existence in a restless and turbulent Africa'. I do not need to recapitulate the events of the past year which have led to Dr. de Kiewiet's statement. Throughout the continent 1960 has been called the year of Africa's freedom. Freedom to do what? Can we expect primitive Africa to develop into a civilized state that has taken millennia of painful effort on the part of other peoples? There is no doubt that it might eventually take place, but is it reasonable to expect this change overnight? The hall-mark of civilized man is the fact of social consciousness — the idea that man does not live for himself alone but also for his fellow man.

We, in the medical profession, understand this full well because our lives are dedicated to just this purpose — serving our fellow man. So far the evidence is that the concepts of democracy and civilization in the new African States are developing painfully slowly. Being in the middle, and being uncommitted to either Eastern or Western blocks, they receive from both sides. What they have contributed to the march of civilization is infinitesimal, even though they form such a powerful block in the United Nations. What they will contribute to mankind in the future is still an unknown quantity. Whatever we think about it, however, it is plain that we who live in the southern tip of Africa have a grave responsibility to keep aloft the torches of science and moral understanding which have come down to us over the ages; and, by our behaviour to the less privileged people amongst us, enable them to enjoy the benefits of our civilization and encourage them to contribute to it. This is our position, and this, indeed, is our destiny. It seems that future generations of South Africans will live or die depending upon the decisions and the character of the people who exist now. We in the medical profession have a very important part to play in the shaping of South Africa's future, and it is essential, therefore, to put our house in order.

Are we satisfied with our achievements in the past, and if not, what are we going to do about it in the future?

### The Present State of our Profession

In accordance with traditional valedictory addresses, I would prefer to give praise to the profession, but, in a desire to be sincere, I feel bound to ask the Association to ponder several questions, notably:

1. Is the quality and quantity of our doctors adequate, as befitting an established civilized community?
2. What have the hospitals of South Africa contributed to modern advances by way of original contributions to the science and practice of medicine?
3. Are we producing a sufficient number of good doctors for our own needs and for our neighbours?
4. What is happening to our younger generation of doctors?

\*Valedictory address, Johannesburg, 21 February 1961.

5. Do we have sufficient courage and drive to play an important part in our own development and that of this continent?

At the risk of being attacked from various quarters, I would say that the quality and quantity of our doctors could, and should, be greatly improved. I would say that, with a few exceptions, the hospitals of South Africa have contributed very little indeed to the modern advances in medicine and surgery. As far as the production of doctors for our neighbours is concerned, we have not enough for ourselves and the situation is worsening by the day. To quote from the survey prepared by the National Bureau of Educational and Social Research of the Department of Education, Arts and Science, which was printed in *Medical Proceedings* of 13 August 1960: 'In the USA, 3% of the profession is engaged in research. In so far as a comparison is permissible, the South African figure is 0.6%'. 'The medical requirements of South Africa will only reasonably be met by something like 4,000 additional practitioners by 1965; whereas the estimated yield from our medical schools will be fewer than 2,000.'

Far from encouraging the furtherance of knowledge, the conservativeness and staleness that permeates thought in the universities, the medical schools, the Federal Council and even the Medical Association, aggravates the present-day position.

The teaching schools are of paramount importance in the development of the profession, yet we find that only one in four applicants can possibly be taken into the University of the Witwatersrand, the only aptitude test being matriculation results which, as everybody knows, is a test of memory rather than intelligence. It is now being suggested that because of the shortage of teachers and facilities, the numbers be reduced by as much as 30%. The senior members of the teaching staffs of our local university will agree with me when I say that the entire future of the medical school is in jeopardy. We are short of doctors, but we do not produce sufficient for our needs because of the difficulties under which the teaching staff labours.

What happens after qualification? Doctors take up various fields of endeavour. Most of them go into general practice and would like to improve their knowledge from year to year. The universities cannot deal with this demand—they have not got the time, the equipment, or the staff, so that the more active members of the profession arrange colleges for general practitioners and postgraduate classes through postgraduate associations.

In the field of specialization, the country is befogged by unimaginative thinking on the part of its leaders. There are a number of examples of our failings in this regard, but let me mention only two or three that strike me.

We find that we cannot provide services in this country which are accepted as common practice in other countries. We have cobalt bombs but we cannot use them because we do not produce the personnel to work with them. There is no adequate system for the training of dermatologists. Not more than two or three dermatologists have been trained in Johannesburg in 30 years since the specialist register came into being. Reconstructive surgery is the basis of all future surgery, because the principles of modern advancements are concerned with repair rather than with elimination. Yet, in the last 20 years, only two reconstructive plastic surgeons have been trained in this country. The result is that there is a shortage of plastic surgeons, and that only a very small percentage of the population are able to obtain the benefits of this type of skilled treatment.

The result of all this is that not only are we creating shortages, but we are actually losing our best young men. Doctors with ambition and a will to get on in the profession, find fulfilment in other countries outside South Africa, since they become frustrated by the restrictions to their development arising from our own outworn

policies. This has not only occurred in the field of clinical medicine, but also in the scientific and laboratory fields, so that we are losing the very teachers that we need so badly. Instead of importing men, we are exporting them. I have no hesitation in saying that this unfortunate state of affairs is of our own making.

#### The Future

Do we have sufficient moral courage and drive to play an important part in our own development and in that of this continent? The answer at present is an emphatic *no*. The South African Medical Council is bogged down by its own regulations and the Federal Council and Branch Councils devote most of their time to the economics of the medical practice and the domestic politics of the profession. Very little time is spent on the improvements in the status of the medical profession in this country. When clinical meetings are held for this purpose, the attendances are very poor, even when distinguished overseas speakers are invited.

Are we going to allow this situation to drift or are we going to take up the challenge on behalf of our country and our own self-respect? This is something that must exercise the mind of every doctor in the country, particularly those representing us in the various councils and associations.

It would be wrong to examine and diagnose the illness that besets the medical profession without putting forward suggestions for its cure, but once an honest appraisal of the situation is made, the treatment should be obvious. What we need more than anything else is positive thinking, particularly on the part of our leaders. We need a new deal, for doctors and patients alike. As a rule, doctors dislike control by lay bodies, but cooperation with lay bodies is essential and our sphere of interest should be broadened to bring them within the general orbit of the welfare of the State. We should not focus our attention only on our own personal problems.

The most important suggestion that I have to make is to broaden the education of medical men—undergraduates, general practitioners, and specialists alike. I feel that the first year at the university should be a postmatriculation year under university conditions, available to every suitable matriculant who wishes to increase the breadth of his education. This would not only assist students and teachers towards the selection of careers, but tend to prevent the squeezing of square pegs into round holes. It would also allow every youngster who feels that he has a calling towards medicine to satisfy that urge for the benefit of himself, the profession, and his country. Every matriculant who feels that he has a call to medicine should be given an opportunity to answer it.

Teachers should not be confined to a closed shop. The entire profession would be glad to assist and, in fact, I can think of nothing better for the general practitioners and the specialists outside the university, than to allow them to teach within the orbit of the university. You have all the teachers you need if you wish to use them. By the same token, smaller hospitals in the country should be invited to supply teaching material and staff. In this regard, I would sincerely recommend the reversion to the honorary appointment system as befitting the dignity and independence of our profession. In point of fact, the best teachers for general practitioners are general practitioners, and the best teachers for specialists who are going to practise outside the walls of the university hospitals, are specialists who practise in this way.

I feel we must take a broad and unselfish view of our obligation to provide a sufficient number of qualified and able people who are willing to do their job, not only for the welfare of the State, but also for the greater weal of those living outside its borders—a factor which may be vital to our future, not only in the immediate future, but for generations to come.

## THE SOUTH AFRICAN MEDICAL CONGRESS, 24 - 30 SEPTEMBER 1961, CAPE TOWN

### HOTEL ACCOMMODATION

The Forty-third Medical Congress of the Medical Association of South Africa will be held in *Cape Town* from 24 to 30 September 1961. Information regarding the Congress is published at regular intervals in the *Journal*. Although it is still relatively early, members who intend coming to Congress are requested to send in their Intention Forms as soon as possible.

Prospective visitors to the Congress are also requested to bear in mind that hotel accommodation in *Cape Town* is somewhat limited and that they should make the necessary reservations well

in advance of Congress. The Travel Bureau of the South African Railways has been appointed the official agent in this connection. Members are requested to contact their local agents who have been extensively circularized in this respect. In the small plateland towns the nearest stationmaster will handle the matter.

Make your reservations now in order to avoid disappointment. In the event of any difficulty, please write to Dr. J. C. Coetzee, Convener, Accommodation Sub-Committee, 43rd South African Medical Congress, P.O. Box 643, Cape Town.

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## ABSTRACT

## A NEW AGENT FOR THE TREATMENT OF VAGINAL CANDIDIASIS\*

The spores of *Candida albicans* are more abundant and more widely disseminated than ever before. Generalized and fatal candidiasis is now being seen in its severest form of infection.

Although pregnancy, diabetes, and previous antibiotic therapy are specific predisposing factors in the aetiology of vaginal candidiasis, the presence of a fungus infection must be suspected in every woman complaining of vaginal irritation, pruritus, or discharge. The classical appearance on examination of a white, caseous or flaky, sour-smelling discharge need not necessarily be present. Many of these patients present a thin, watery, sometimes brownish discharge which appears to arise in an acutely congested vaginal mucosa. The culture of the vaginal secretions on Nickerson's medium produces characteristic brown or black colonies after incubation for 2 or 3 days at room temperature. This is a very simple, inexpensive, and accurate office diagnostic procedure.

The numerous agents which have been used in the treatment of vaginal candidiasis include gentian violet, silver picrate, acetic acid, propionic acid, various proprietary arsenical compounds, nifuroxime, phenylmercuric acetate, and nystatin.

The agent used in the study by Dr. Lapan is chlordanol. It has excellent activity *in vitro* against all of the pathogenic fungi, yeasts, and actinomycetes tested. In dermatologic fungus infections, it has a high degree of efficacy, and its acceptability is enhanced by its lack of staining. Chlordanol was initially used with excellent therapeutic effect in the form of vaginal insert tablets, each containing 100 mg. of the active substance in a 2-G. lactose base; it was also incorporated in a cream base ('sporostacin cream'). This cream was in a 1% concentration, and each applicator contained 50 mg. of the active ingredient. The majority of patients in the study were treated with this cream formulation.

\* From an article by Bernard Lapan, M.D. in *American Journal of Obstetrics and Gynaecology*, vol. 78, p. 1320.

Only women with positive vaginal cultures on Nickerson's medium were included. Thirty-one such patients were observed and treated. They were instructed in the vaginal insertion of either the tablets or 5 c.c. of the cream, by means of disposable plunger applicators, twice daily for a period of 14 days. One week after the completion of treatment a repeat culture was taken. If the culture remained positive, a repeat course of treatment was given. During the acute phase of the infection, coitus was prohibited. No douches were permitted, and the patients were instructed not to use soap in the region of the vulva.

Of the 31 patients treated, all reported relief of the symptoms of vaginal discomfort within 2 days. Many stated that improvement began within a few hours after the first vaginal application of the drug. The associated intertrigo seen in some cases also disappeared rapidly. The Nickerson's cultures remained positive, however, and this required a second course of treatment in 15 of the 31 cases. After the 2 courses of treatment, all patients were normal except 2 and these women were given third courses of treatment with chlordanol. The side-effects noted were minimal.

The use of this new compound, chlordanol, in the treatment of vaginal candidiasis offers the advantages of simplicity and rapid relief of symptoms, together with a high percentage of culture-free cures.

Although other substances are available for the treatment of vaginal candidiasis, chlordanol will take its place with them as one of the most rapidly effective and dependable of all. Its use should also find acceptance in the prophylaxis of vaginal candidiasis in women receiving broad-spectrum antibiotic therapy, as well as in the prevention of neonatal *Candida* infections.

Since submitting his article for publication, the author has treated over 125 additional cases of vaginal candidiasis, and has obtained culture-free cures in all but 4 instances.

## PASSING EVENTS : IN DIE VERBYGAAN

Members are reminded that they should notify any change of address to the Secretary of the Medical Association of South Africa at P.O. Box 643, Cape Town, as well as to the Registrar of the South African Medical and Dental Council, P.O. Box 205, Pretoria. Failure to advise the Association will result in non-delivery of the *Journal*. This applies to members proceeding overseas as well as those who change their addresses within the Union.

University of Cape Town and Association of Surgeons of South Africa (M.A.S.A.), Joint Lectures. The next lecture in this series will be held on Wednesday 10 May at 5.30 p.m. in the E-floor Lecture Theatre, Groote Schuur Hospital, Observatory, Cape. Mr. A. J. Walt will speak on 'Benign disease of the breast'. All members of the Medical Association are welcome to attend this lecture.

The South African Institute for Medical Research, Johannesburg, Staff Scientific Meeting. The next meeting will be held on Monday 15 May at 5.10 p.m. in the Institute Lecture Theatre. Dr. S. Krawitz will speak on 'Radio-isotope surface counting techniques in haematologic diagnosis'.

Medical Students' Council: 1961 Refresher Course. A refresher course will be held in Durban for the week 3-9 July 1961, for clinical year students in particular, and any pre-clinical students who may wish to attend. The course will be on normal physiology and the changes leading to pathology, and subjects relating to the various systems, e.g. central nervous system, cardio-vascular

system, digestive system, respiratory system, and urinary system will be discussed; one day being devoted to each system.

The course will be conducted by members of the Medical Faculty of the University of Natal, and by practitioners in Durban. Lectures will be given in the mornings, followed by clinical meetings and discussions in the afternoons and evenings. Accommodation can be arranged at the University residences, and the cost including train fare and accommodation is approximately R20. The fee for attending the course will be R1. Further information may be obtained from the local offices of the Medical Students' Council at Cape Town, Durban and Johannesburg.

University of the Witwatersrand, Medical Graduates Association. At the Annual General Meeting held at the end of March, the following were elected to office: Dr. L. Slutskyn, President; Dr. I. Norwich, Vice-President; Dr. A. Porter, Hon. Treasurer; and Dr. H. Cohen, Hon. Secretary.

Dr. L. M. Marchand, Associate Secretary of the Association, is proceeding overseas early in May on three months' leave, accompanied by Mrs. Marchand. During his absence all correspondence normally addressed to him on contract practice matters should continue to be sent to the Association's Pretoria office (P.O. Box 1521, Pretoria) where it will receive attention.

Dr. L. M. Marchand, Medesekretaris van die Vereniging, vertrek vroeg in Mei op 'n oorsese vakansietoer van drie maande. Mev. Marchand sal hom vergesel. Gedurende sy afwesigheid moet alle korrespondensie wat in die gewone loop van sake oor kontrakpraktykwerk aan hom gerig word, na die Vereniging se kantoor te Pretoria gestuur word (Posbus 1521 Pretoria), waar dit aandal sal geniet.

## THE BENEVOLENT FUND : DIE LIEFDADIGHEIDSFONDS

The following donations during March 1961 are gratefully acknowledged:

Met dank word die volgende skenkings gedurende die maand Maart 1961 erken:

*Votive Cards in Memory of: Geloftekaarte ter Nagedagtenis aan:*

Dr. R. H. Rose-Innes by Dr. and Mrs. H. J. Louw; Dr. Pat Thornton by 'The old staff of Westfort'; Mr. F. R. Elton by Dr. J. P. Immelman; Michael Falcon by Dr. A. J. Orenstein; Mr. P. J. Fowler by Dr. J. T. M. de Villiers; and Dr. S.A. Lange by Dr. W. E. Laufer.

Total Received from Votive Cards: R18.50  
Totaal Ontvang van Geloftekaarte:

*Services Rendered to: Dienste Gelewer aan:*

Mev. A. Kirsten deur Prof. J. N. de Villiers, Dr. C. G. G. du Plessis, Dr. Lowna Keet, Dr. J. J. de Wet en Dr. D. Krige.

Dr. M. Campbell-Mackie by Dr. M. H. Lunitz.

Dr. B. Israel by Dr. S. J. Hoffman, Dr. S. Hoffmann, Dr. I. J. Balkin and Dr. H. Jackson.

Mrs. P. Vallentine by Dr. L. J. Abramowitz.

Mev. P. D. Nel deur Dr. Jacques Roux.

Mev. Beck de Villiers deur Dr. C. F. Marais, Dr. F. P. Scott, Dr. I. J. Venter en Dr. C. Albertyn.

Dr. G. F. C. Troskie deur Dr. A. M. le Roux.

Dr. H. E. Bernstein and family by Dr. S. H. Fine, Dr. R. J. H. McMahon, Dr. N. Kemsley-Pein and Mr. B. A. Armitage.

Mrs. D. Villet by Dr. L. Lane.

Dr. W. E. Laufer by Dr. H. O. Hofmeyr and Dr. H. R. Libermann.

Total Received from Services Rendered: R152.00  
Totaal Ontvang van Dienste Gelewer:

*Donations: Skenkings:*

Drs. I. Friedman, P. L. Botha, A. Katz, A. L. Burman, J. P. de Villiers, A. R. Malherbe, H. Saacks, P. F. Venter, G. L. Were, H. L. Dippenaar, F. E. Meltzer, E. Meltzer, G. P. J. v. Niekerk, F. Krone, S. Sagor, F. A. v. Heerden, A. G. Chene, C. C. Akerman, R. K. Beardmore, L. R. Tibbit, L. C. Prozesky, M. J. F. Davis, D. A. Hoffmann, S. S. Hoffmann, H. E. Bernstein, H. A. Kalley, E. Briggs, D. G. Cowie, C. Akerman, J. R. Clacey, P. T. Hauff, B. A. Armitage, F. R. W. K. Allen, J. D. M. Barton, J. D. Lumsden, A. I. Pitcher, W. Blignaut, C. R. Hallot, J. S. Barnes, C. L. Wicht, M. Mauter, D. S. Palmer, C. A. N. Ovendale, R. St. C. Sinclair, F. L. Potter, D. S. Gardner, W. J. Perkins, J. H. Boshoff, B. B. Bertin, H. Simon, M. T. S. Conradie, H. P. G. Militz, L. Brown, J. H. Labuschagne, C. M. Kmietsch, J. K. McKechnie, J. Grieve, V. A. v. d Hoven, A. F. F. Maske, T. H. Jackson, C. F. Scheepers,

R. Theron, M. L. Cohen, E. Tucker, C. B. J. Bester, L. G. MacKenzie, M. Minde, W. Fabian, P. J. Grobler, S. Kahn, R. J. D. Jamieson, G. W. Moggridge, A. H. Baxter, P. A. Clarke, P. J. H. McMahon, J. R. Reznick, N. H. Helman, J. P. Beazley, H. Bell, W. L. Robertson, H. M. Fyvie, H. S. Edwards, R. G. de Kock, B. C. Freyer, C. H. Botha, R. J. Marot, J. de V. Meiring, D. S. McCall, A. C. L. Grantham, J. M. Calitz, S. H. Cohen, T. H. Whitsitt, F. E. Bamford, N. K. Pein, J. O. Matthews, A. G. W. Farrell, P. V. MacGarry, H. J. J. Beyleveld, S. Grodd, L. Tomory, R. P. Stafford, A. Nel, A. L. Wilson, J. C. W. Ehlers, Prof. E. C. Crichton, and Drs. Harris, Kuschke and Hofmeyr.

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Total .. .. .	134.55
Dr. M. Campbell-Mackie .. .. .	4.75
Dr. R. McDonald .. .. .	5.00
Dr. C. W. Coplans .. .. .	10.00
Dr. J. L. v. Selm .. .. .	4.75
Dr. A. W. S. Sichel .. .. .	5.25
Dr. E. C. A. Fristedt .. .. .	5.00
Dr. R. J. Laubscher .. .. .	10.00
Dr. P. J. Malan .. .. .	5.25
Dr. J. A. Greyling .. .. .	20.00
Dr. H. H. Bloch .. .. .	4.00
Dr. B. Navid .. .. .	4.00
Dr. J. K. McCabe .. .. .	4.00
Dr. J. M. Hoffman .. .. .	6.00
Dr. M. I. Seedat .. .. .	5.95
Mr. T. A. Currie .. .. .	7.25
Dr. R. Le G. Smith .. .. .	4.35
Dr. A. W. H. Cheyne .. .. .	5.75
Dr. J. J. C. Hofmeyr .. .. .	4.20
Proceeds Alan Sichel Golf Tournament (Cape Western Branch M.A.S.A.) .. .. .	33.00
Cape Western Branch (M.A.S.A.) Collection Box .. .. .	11.78
Bequest Late Mr. B. L. Goldschmidt .. .. .	200.00
Total Donations: Totale Skenkings .. .. .	R494.83
Grand Total: Groot Totaal .. .. .	R665.33

## PHARMACEUTICAL NEWS : FARMASEUTIESE NUUS

### ORAL DIURETICS IN CLINICAL MEDICINE

The arrival of a new Squibb medical film, 'Oral Diuretics in Clinical Medicine', is announced by Squibb Laboratories (Pty.) Limited.

For the practicing physician, the problem of oedema—whether of renal, cardiac, or hepatic origin—is one which he constantly meets. For years the search has continued for the ideal diuretic agent, one with a low capacity for electrolyte upheaval and a sustained action, a drug free of allergic or toxic reactions in usual dosages.

This film begins with a brief, diagrammatic review of normal renal physiology, delineating the three compartments—cells, vascular system, and extracellular spaces—in which body fluid is proportionately contained. Sodium is stressed as being the critical water-retaining ion in preserving the correct proportions of protein, organic acids and electrolytes for maintaining homeostasis. When renal dysfunction occurs, retention or increased reabsorption of water and sodium results in oedema, which is thus the common denominator of a variety of diseases.

Different approaches to the treatment of oedema are discussed.

Reduction of sodium intake is one method. However, more successful therapy involves the elimination of sodium and water. The various diuretic agents, their advantages, disadvantages and modes of action are described. Although the parenteral organic mercurials are powerful and consistently effective, with a long history of usefulness, recent years have seen the advent of oral diuretics which are effective and safe as well as being easy to administer. The benzothiadiazines, termed 'natriuretic agents' because they increase primarily the excretion of sodium and water, have been found to be the most potent and dependable of these. They act directly on the renal tubules to depress sodium and water reabsorption.

The last part of the film introduces reports and case histories to indicate the effectiveness, safety and convenience of one of the benzothiadiazine compounds in various conditions involving oedema—also its usefulness in the treatment of hypertension.

Application for loan of this 16 mm. colour, sound film should be made to Squibb Laboratories (Pty.) Ltd., P.O. Box 48, Isando, Transvaal, telephone 975-4614.

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## IN MEMORIAM

WILHELM JACOBUS ADRIAN MOSTERT, M.B., CH.B. (PRET.)

Dr. M. G. van Niekerk, van Bronkhorstspuit, skryf:

Die skielike heengaan van dr. Mostert aan kroonslagader-trombose aan sy woning te Somerset-Wes op 21 Maart 1961, het al sy vriende en kollegas diep geskok.

Dr. Mostert is gebore op 30 Junie 1918 in die Strand. Sy moeder het hy reeds op die vroeë ouderdom van 5 jaar verloor en hy het by 'n tante op George ingewoon, waar hy dan ook sy skoolloopbaan aan die Outeniqua voltooi het. Na die matrikulasie-eksamen is hy na die Opleidingskollege, Paarl, waar hy hom bekwaam het as onderwyser. Hy het 4 jaar lank onderwys aan die Hoërskool Maitland gegee waar hy aktief aan buitewerke aktiwiteite deelgeneem het. Onder andere het hy in die eerste span rugby gespeel vir Kuilsrivier en Maitland. Hy was ook die stigter van die C. J. V. Dirkie Uys, waarvan hy ook voorsitter was.



Dr. Mostert

Dr. Mostert, beter bekend as Mossie, het sy mediese kursus gedurende Februarie 1944 aan die Universiteit Pretoria begin waar hy al gou 'n baie belangrike rol begin speel het in die verskillende studente-aangeleenthede. Hy het gedien op die studenteraad en was die besonder gewilde voorsitter en leier van die groep wat aan die einde van 1949 gekwalifiseer het. Hy het sy universiteit ook drie jaar lank aangevoer as dirigent; sy bekwaamheid en kwinkslae met intervensie sal deur menigeen nog lank onthou word.

Ná voltooiing van sy huisdoktersjaar aan die Algemene Hospitaal, Pretoria, het hy 10 jaar lank op Rustenburg gepraaktiseer, waar hy hom onderskei het as 'n baie bewaamde algemene praktisyn. Alhoewel sy bloeiende praktyk baie tyd en aandag geveer het, het hy ook nog tyd gevind om die gemeenskap op ander gebiede te dien. Hy het gedien as Voorsitter van die Wes-Transvaalse Tak van die Mediese Vereniging, President van die Gholfklub, Direkteur van 'n plaaslike maatskappy, en as bestuurslid van SABRA.

Een van sy groot ideale is vir 'n korte duur verweselik toe hy na sy geliefde Kaapland kon terugkeer om hom as algemene praktisyn op Somerset-Wes te vestig in Maart 1960.

Dr. Mostert sal onthou word as 'n bewaamde algemene praktisyn wat die probleme wat met die praktyk gepaard gaan, blymoedig gedra het en wie se opregte menslikheid veel daartoe bygedra het om die laste van sy medemens te verlig.

Die heengaan van Mossie laat 'n groot leemte onder sy vriende en kollegas, en ons wil ons diepste meegevoel betuig met sy eggenote, Amy, en hulle kinders Linda, Annette, Ilse en Willie.

NEW PREPARATIONS AND APPLIANCES:  
NUWE PREPARATE EN TOESTELLE

## ASTIBAN

Roche Products (Pty.) Limited announce the introduction of Astiban, and supply the following information:

**Composition.** Astiban is antimony dimercapto-succinate sodium salt (TWSb/6), containing 25-26% trivalent antimony. Antimony is bound to the sulphur atoms forming a complex ring structure which has a higher degree of stability than the corresponding oxygen/antimony structures in tartar emetic, catechol, and gluconic acid derivatives. The stability of the ring structure containing the antimony is related to the degree of toxicity of this compound.

In Astiban the antimony is about 30 times less toxic than tartar emetic, as shown in animal experiments.

**Acute toxicity.** The lethal dose of Astiban and tartar emetic was determined in mice: Astiban subcutaneously 90%, 3,500 mg./kg. Tartar emetic subcutaneously 90%, 29 mg./kg.

**Subacute toxicity.** Astiban is to be used in the treatment of *S. haematobium* and *S. mansoni*. In large-scale clinical trials it has shown its usefulness in, firstly, curative treatment and secondly, the management of suppressive treatment.

**Dosage and administration.** Astiban should be administered according to the body weight. The total dose in adults lies between 30 and 50 mg./kg. with a maximum of 2.5 g. In children under 20 kg., total doses of 40-60 mg./kg. may be given. The higher doses are indicated in *S. mansoni* infestation.

**Route of application.** The intramuscular route is preferred, giving a deep injection into the upper outer quadrant of the buttock. Astiban can, however, be used for intravenous injection if desired.

**Tolerance.** Depending on nutritional status, geographical environment, load of schistosomes and other helminths, tolerance can be considered as very satisfactory. **Note:** When injections are given on consecutive days, more side-effects are observed. By extending treatment over 6 to 9 days using the alternate-day schedule, better tolerance is sometimes obtained without significant decrease in the therapeutic effect.

**Side-effects.** These include anorexia, nausea, and vomiting; abdominal discomfort; joint and muscle pains; occasionally activated or latent pyogenic viral or fungal infections; and skin rashes, herpes, and interdigital pruritis. In the proposed dosage, Astiban has occasionally produced alterations in T waves, but it is not known to affect the cardiovascular, hepatic, or renal functions. **Note:** The above side-effects are mostly benign and transitory and disappear after a short while without after-effects.

**Contra-indications.** Active tuberculosis, pyogenic infections, febrile conditions, congestive cardiac failure, hepatic insufficiency, jaundice, herpes, massive intestinal helminthic infestations (these should be cleared up first with appropriate anthelmintics before starting Astiban treatment; santonin, however, should not be used).

**Presentation.** Astiban is presented as a pale-yellow dry powder in sterile rubber-capped vials containing 2 g. of the active substance. 20 ml. of pyrogen-free sterile water should be added as a solvent immediately before use. The dissolved substance has limited stability, but can be stored in refrigerators and used as long as it remains transparent and practically colourless. Each vial of 2 g. represents the average optimal dose per case.

**Distinctive features of Astiban.** (1) Short duration of treatment, (2) high presumptive cure rate, (3) satisfactory tolerance, (4) applicable by the intramuscular route, (5) suitable for ambulant treatment, (6) reduction of hospitalization days since daily injections can be given, and (7) indicated for mass treatment and suppressive management of schistosomiasis.

Further information may be obtained from the Scientific Department of Roche Products (Pty.) Limited, P.O. Box 6158, Johannesburg.

## ESKORNADE SPANSULE CAPSULES

SKF Laboratories (Pty.) Ltd. announce the introduction of Eskornade and supply the following information:

**Composition.** Eskornade is made up of Isopropamide Iodide 2.5 mg., Phenylpropanolamine HCL 50.0 mg., and Diphenylpyraline HCL (Histryl) 5 mg.

**Description.** Eskornade is a unique triple-acting preparation which contains a special drying agent in addition to a decongestant and an antihistamine. Isopropamide iodide, the drying agent, reduces excessive lacrimation and hypersecretion of mucus. The decongestant, phenylpropanolamine, reduces a vascular engorgement and often permits blocked sinus cavities to drain. The antihistamine, 'histryl', reduces sneezing, rhinorrhea, and also itching of the eyes. Acting together, these three agents combine to provide outstanding relief from upper respiratory distress.

**Indications.** Congestion and hypersecretion in the nasal and paranasal sinuses associated with: the common cold, nasal allergy, acute and chronic rhinitis, influenza and sinusitis.

**Advantages.** The therapeutic effect of Eskornade begins promptly

and, because it is a 'Spansule' sustained-release capsule, continues for 10 to 12 hours with a single dose.

**Contra-indications and side-effects.** Glaucoma and prostatic hypertrophy. Use cautiously when severe hypertension is present. Side-effects are slight and transient. These include dry mouth, drowsiness, insomnia, and blurred vision.

**Dosage.** For adults and children over 12: One Eskornade Spansule capsule every 12 hours.

**Presentation.** Eskornade Spansule capsules are available in containers of 30.

Further information may be obtained from: SKF Laboratories (Pty.) Limited, P.O. Box 38, Isando, Transvaal.

#### NAVIDREX TABLETS

Ciba (Pty.) Ltd. announce the introduction of Navidrex (cyclopenthiiazide)—a benzothiadiazine derivative but *not* 'just another oral diuretic'. Milligram for milligram it is the most potent and most economical sali-diuretic that has ever been offered to the medical profession.

**Description.** Each tablet contains 0.5 mg. of 3-cyclopentyl-methyl-6-chloro-7-sulphamyl-3, 4-dihydro-1, 2, 4-benzothiadiazine 1, 1-dioxide.

**Indications.** Navidrex can be employed in all conditions for which sali-diuretics are indicated. It has its own antihypertensive effect and may with advantage be combined with more powerful

anti-hypertensive agents such as 'serpasil', 'adelphane' and 'ismelin', which can then be used in lower dosages than if employed alone.

**Contra-indications.** Navidrex should not be used in cases of hepatic pre-coma and coma.

As with other sali-diuretics, Navidrex may sometimes precipitate an attack of gout during periods of remission in gouty patients or in patients predisposed to gout.

**Advantages.** Unmatched potency in microgram doses, unrivalled economy in use, unexcelled tolerability, minimal effect on potassium reserves, ideal 12-hourly duration of action, and simple dosage schedule.

**Dosage.** To ensure a strong diuretic response one tablet (0.5 mg.) should be given daily.

To any patients suffering from extensive oedema, in whom it is desired to achieve massive diuresis, it would certainly be preferable to prescribe two tablets (1.0 mg.) daily for the first few days. Once the oedema has been resolved, one tablet (0.5 mg.) daily should prove sufficient.

For chronic maintenance therapy, one tablet (0.5 mg.) every second or third day or, alternatively, half a tablet (0.25 mg.) daily. During prolonged therapy supplementary potassium is advised.

Further information may be obtained from Ciba (Pty.) Limited, P.O. Box 5383, Johannesburg.

#### BOOK REVIEWS : BOEKBESPREKINGS

##### THE CELL OF SCHWANN

*The Cell of Schwann.* By Gilbert Causey, M.B., F.R.C.S. Pp. 120+xi. 40 figures. 21s. net + 1s. postage abroad. Edinburgh and London: E. & S. Livingstone Ltd. 1960.

Specialized monographs appear with greater and greater frequency these days and they are seldom of interest to anyone who is not directly concerned with the speciality discussed. This little book, however, should be read by medical scientists, clinicians, neurosurgeons, and pathologists.

Knowledge of the cell of Schwann has become increasingly important in recent years because of its connections with myelina-

tion, regeneration, and neoplasms of nerves, and Professor Causey provides up-to-date knowledge in an eminently readable manner. Although to a certain extent this is a review, it is a review in the best manner; critical, analytical, and spiced with personal findings and observations.

The photographs and diagrams are excellent and the presentation of the volume, as always from this publisher, is of the finest.

A comprehensive bibliography adds to the value of the book which is highly recommended to all who are interested in the nervous system.

A.G.R.

#### CORRESPONDENCE : BRIEWERUBRIEK

##### GLUCOPHAGE IN DIABETES MELLITUS

*To the Editor:* In our recent article in this *Journal*<sup>1</sup> we pointed out that the diguanides are generally believed to act by inhibiting certain enzymes which take part in oxidative glycolysis in the tricarboxylic cycle.<sup>2</sup>

Messrs. Rona Laboratories have sent us this further information regarding the mode of action of glucophage (official name, 'metformin').

'Dimethyldiguanide has been investigated experimentally and no such inhibitory effect on aerobic respiration observed. On the contrary, Sterne has produced evidence to show that it has an antiketotic activity, though not as powerful as that of insulin. It seems that the mode of action of dimethyldiguanide is related to the stimulation of aerobic respiration, and it may act by potentiation of insulin peripherally.'

If this is confirmed, the mode of action of 'metformin' may be more physiological than we previously thought.

J. B. Herman  
W. P. U. Jackson

401 Grand Parade Centre  
Cor. Adderley and Castle Streets  
Cape Town  
24 April 1961

1. Herman, J. B. and Jackson, W. P. U. (1961): S. Afr. Med. J., 35, 14.
2. Hollunger, G. (1955): Acta pharmacol. et toxicol., 2, suppl., 1.

##### TELEGRAM TO PRIME MINISTER

*To the Editor:* I strongly agree with Dr. L. E. Miller's letter in the issue of the *Journal* of April 1961. I, too, am amazed that the

South African Medical and Dental Council should have sent a congratulatory telegram to the Prime Minister.

It naturally signifies their endorsement of the views of one particular political party. That is their concern, but unfortunately it is taken to mean that it is the opinion of the Medical Association as a whole.

Jeppe Street  
Johannesburg  
11 April 1961

Stephen Eisenhammer

##### TELEGRAM TO PRIME MINISTER

*To the Editor:* I cannot see why anyone should object to the telegram sent to Dr. Verwoerd by the South African Medical and Dental Council.

Allow me to remind all disappointed correspondents that we certainly do not all hold the same viewpoints. Even then, when the Prime Minister left the country for the Commonwealth conference, he did so, not as the representative of the Nationalist Party, but as the spokesman for the whole nation and supported by all parties in Parliament.

Let me remind you that there are, and always will be, many clear-thinking members on the Council. We regard the telegram as a gesture of goodwill and appreciation for the way our Premier managed to hold his own against the onslaught of world opinion.

J. T. Rossouw

716 Harley Chambers  
Jeppe and Kruis Streets  
Johannesburg  
19 April 1961